COLLECTED PAPERS

of

THE MAYO CLINIC

ROCHESTER, MINNESOTA

EDITED BY

Mrs. M. H. MELLISH

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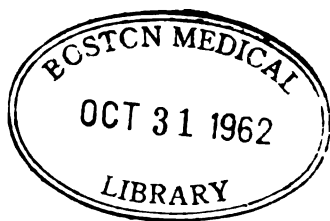
FOREWORD

THE increasing number of papers now being published annually from the Mayo Clinic has made it seem expedient to abstract for the present volume some of the articles the material of which has been partially covered in this or in previous volumes. In some instances papers here presented are part of a series of studies which have appeared in earlier volumes or are to be continued later. Where papers have been thus grouped an effort has been made to abridge repetitions that were necessary when the study was first presented. It is hoped that this method will serve to give a clearer conception of the relationship of researches on one subject by the same investigator as well as to reduce the size of the volume.

ROCHESTER, MINNESOTA.
   May, 1915.

FOREWORD TO VOLUME 1905–09

MANY of the papers herein collected have been read before various medical societies, and all of them have been published in current medical literature. Our chief reason for bringing them together in the present form is for our own convenience of reference; an object which has been greatly furthered by the detailed index supplied by the publishers. Our first plan was to have the papers printed for private distribution only, but at the instance of numerous members of the medical profession we have consented to having the book placed on the market. We trust that it will be accepted for just what it purports to be, namely, an indexed collection of reprints.

THE AUTHORS.

ROCHESTER, MINNESOTA.

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ALIMENTARY CANAL

MOUTH INFECTION AS A SOURCE OF SYSTEMIC DISEASE *

CHARLES H. MAYO

It has taken a long time for the general public to appreciate the full rôle of infection in the production of death, while even in the medical profession more has come from the study of infections in the prevention of disease than in increasing the means of cure of disease, great as have been the results of treatment.

Since all animal life depends on some other form of cell life, vegetable or animal, it seems but the part of all life to carry on this process of germinative development and maturity. It is only the resistance of healthy cells that prevents the inroads of the myriads of ever-present bacteria and animal parasites which are striving to get a foothold that they may in turn carry on their life-work. Disease, then, is an inflammatory process from infection and the efforts at repair. It may also be chronic from the failure of cell life through lack of defense, from defective nutrition and advancing age.

We still speak more or less lightly of the so-called diseases of childhood, and the time is not far past when mothers took their children to be exposed to whooping-cough, mumps, etc. To-day the intelligent woman knows that it is not necessary that the vitality of the child should be jeopardized by such preventable diseases, and that when they occur, it is through carelessness, neglect, or ignorance on the part of some one.

A comparatively small number of infections occur through wounds of the cutaneous surface. Many of those affecting the

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special organs are incurred through direct or indirect contact, as those of the eye and of the genito-urinary system. They may make most serious inroads on the general health. Infections which produce the greatest number of diseases enter the system by way of the alimentary and respiratory tracts. Somewhere in the line, then, of the alimentary and respiratory tracts and in the excretory ducts of the body lie the sources of the entrance of organisms which terminate life in the majority of instances. The great importance of the well-known diseases of the nasal passages, with their sinuses, the lymphoid tissue of the pharynx, including the tonsils, and the diseases of gums and teeth, which have been given prominence by the dental profession during the last three years, is now more generally appreciated.

The mouth is the harbor of many varieties of bacteria which are constantly taken into the stomach during the process of eating. We have long looked on the acids of the stomach as destructive to such bacteria, but Smithies, in a microscopic examination of gastric extracts from 2406 different individuals with "stomach complaint" (dyspepsia, indigestion, and the like), showed that, irrespective of the degree of acidity of such gastric extracts, bacteria were present in 87 per cent. Morphologically cocci and diplococci were present in 83 per cent.; short and long rods (often of the colon group), in 58 per cent.; typical streptococci and staphylococci, in 17 per cent., and Leptothrix buccalis in 24 per cent. In 54 cultural studies of saliva from "dyspeptic" patients streptococci and staphylococci were demonstrated in over 80 per cent., bacilli in 66 per cent., and Leptothrix buccalis in more than 14 per cent. Comparing these figures, it would appear that the common forms of pus-producing organisms (streptococci and staphylococci) have their proliferation retarded in gastric juice, but that bacilli (often of the colon group), as well as Leptothrix buccalis, thrive in the stomach.

Bacteria of various forms live in the small intestine, or at least pass through it or into the blood-stream by way of the mucous membrane. They exist in such great numbers in the large bowel that, whether living or dead, they constitute a con-

siderable bulk of the dejecta. During the last few years some important points have been added to our knowledge of bacteria. Living germ life in the blood, or bacteremia, occurs in all infectious diseases. According to their number and virulence, the blood responds in slight or extreme degree to the symptoms, general and local, constituting the disease.

We have long known that bacteria were specified in type and action in all diseases in which we have been able to identify a specific germ. Rosenow has done a great work in showing that changes in environment may so change bacteria that specific action varies. The appearance of the bacteria is also unlike that of the original cell. In the blood-stream these various forms, once they enter it, are selective in choosing their location, thereby developing specific local disease. The old "idiopathic" osteomyelitis of the child we now know may follow a short time after a specific tonsillitis. Pyorrhea, tonsillitis, or sinus disease may be the source of an infection which we call rheumatism. Root abscesses and pus pockets connecting with them are often the source of acute and chronic rheumatism. The nasal sinuses and chronic mouth and throat infections develop anaphylaxis from the constant poisoning, and their results are shown in hay-fevers, asthmas, urticarias, etc. Rosenow's work is going far to show that ulcerations of the stomach are conditions in which the mucosa is attacked from behind through the blood-stream by bacteria which live in the blood and have a selective affinity for these particular areas. Septic bile, which, in the majority of instances, is caused by infection, is carried to the liver through the portal circulation. It creates such changes in the bile that it fails to activate the pancreatic and duodenal secretion, thus making various phases of indigestion, with qualitative rather than quantitative food trouble. Lower down we have the appendix, with its lymphoid tissue, which approximates in character that of the tonsil. Here the acid types of bacteria have the same opportunity, could they but enter the blood-stream, of making erosions of the gastric mucosa as the specific form which is found in the mouth. We may here note that acid-secreting or acid-bathed surfaces are very subject to

cancerous change, while alkaline-bathed surfaces are much less liable to be involved. Saliva is neutral or slightly alkaline in health, yet less than 20 per cent. of people have healthy mouths. The infected mouth shows a tendency to the acid reaction, and it is through this acid change that we have an additional danger in cell degeneration, of malignant type, from chronic irritation.

The stomach is the most common location of all cancers, while the alkaline small intestine is rarely subject to cancer and the duodenum is most resistant to it. The large bowel again reverts to an acid reaction and is very subject to cancer. So also is the bladder. These structures with acid secretion are of more recent development than are many tissues of animal life, several of them being classed as organs of convenience, which fact renders them possibly less resistant.

Certainly enough is known concerning infections and their mode of entrance, so that the infected and diseased mouth and respiratory tract must be looked on as most serious menaces. Much may be done by more general and effective school inspection. The present generation of children will understand and demand protection for their children in time. The first teeth should be watched, that the second be not permitted to erupt irregularly, causing deformities. Jaws should be spread that the teeth may meet and the high arched palate, diminishing nasal breathing, thereby reduced. Tonsils and adenoids should be looked after, thus preventing ear and mastoid diseases, rheumatism, endocarditis, etc. In chronic and recurring diseases a search must be made to establish positively the non-participation of each of the several sources of infection.

The physicians engaged in this line of observation require fully as much training in the rudiments of dentistry as the dentist does in the signs of infectious diseases. While we have leaders in all professions, through the energy of their kinetic glands, the "big stick" which leads to our advancement is in the hands of the progressive and educated public who are constantly demanding more of their dentists, of the medical profession, and of the state in protecting them against preventable diseases.

TONSILLECTOMY IN THE TREATMENT OF CHOREA *

ALEXANDER ARCHIBALD

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We are all familiar with the fact that pathologic tonsils, especially in children, produce many serious and often fatal infections. In examining children it is important that the tonsils and upper air-passages should not be forgotten; in fact, that they should be scrutinized carefully. A very satisfactory examination may be obtained by retracting the anterior pillar of the fauces, though even with this procedure a diseased tonsil may not be recognized visually. It is only when they are massaged with a finger that pus or caseous material exudes and comes into view.

Of the various diseases probably having their origin from the tonsils, the rheumatic infections are among the most important. It has long been a well-recognized fact that chorea is intimately associated with the rheumatic infections, and, although this knowledge depends chiefly upon clinical observations, the evidence obtained is convincing. The following are salient points of evidence as seen from the cases examined at the Mayo Clinic and those recorded in the literature: (1) The frequency of a previous history of tonsillar disease in rheumatism and chorea; (2) the frequent occurrence of the two diseases together, or at different times in the same individual; (3) the liability of the two diseases to be complicated by cardiac affections.

Of late this evidence has been materially strengthened by bacteriologic experimentation. Rosenow's work, for example, has clarified our ideas with regard to rheumatic infection. He has

proved conclusively that definite strains of the same organism have a predilection for special tissues and organs, and it would seem probable that chorea is also produced by a strain of streptococcus which has a special tendency to attack the central nervous system.

Dick and Rothstein[1] have announced that an article dealing with this subject will soon be published. They stated that a streptococcus from the tonsils of a patient who had chorea for five years was injected into a dog which, within twelve hours, developed choreic symptoms. They also have stated that similar organisms have been isolated from a number of more acute cases of chorea. This is strong proof that a streptococcus is responsible for the production of chorea.

Notwithstanding the fact that physicians have recognized the close relationship between the acute rheumatic infections and chorea, and that both are associated with diseased tonsils in a great majority of cases, most writers on the subject fail to deal with the tonsils in the treatment of chorea. Numerous drugs have been recommended, especially sodium salicylate and arsenic. Absolute rest, however, is always the main object in the treatment. On reviewing the literature I find that Wilson[2] mentions a few men who emphasized the removal of pathologic tonsils, and in cases where this had been done the results had apparently been very gratifying. For many years tonsils have been removed in children presenting a picture of rheumatic infection with perhaps a history of chorea; but it is only within the last two or three years that a few men have advised and practised tonsillectomy as an essential procedure in the treatment of chorea.

In 1911 Giffin[3] suggested tonsillectomy in chorea, even if the patient was at the height of an attack. This suggestion followed the observation of cases at the Mayo Clinic in which the frequency of diseased and hypertrophied tonsils, together with a past history of tonsillitis, was noted in association with chorea.

In some cases it is very difficult to get definite information of sore throat in children. Often on examination we find strong evidence of infection in the tonsils, though the patient gives no definite history of having suffered from sore throat.

In reviewing our cases of chorea, I found that 11 have had tonsillectomy performed during the last three years. Of this number, reports of the present condition have been obtained from 7. I shall, therefore, confine my discussion to these.

CASE 1 (40591).—E. E. G. Girl, aged nine, was seen in August, 1911. Previous to partial tonsillectomy in July, 1910, she was very delicate and had had frequent tonsillitis. During the last three months she had become very nervous and her family physician made a diagnosis of chorea. Examination showed the child to be thin and pale, with slight choreiform movements of the hands, large adenoids, and a diseased fragment of the right tonsil. The tonsil and adenoids were removed in August, 1911. A letter, July 25, 1914, i. e., three years later, reported her greatly improved but still somewhat nervous. There was no recurrence of chorea. How soon after operation the choreiform movements ceased was not learned.

CASE 2 (A84537).—M. S. Girl, aged sixteen, was examined in May, 1913. History of attacks of tonsillitis, the last attack one year ago. She had had severe attacks of chorea, lasting three to fifteen days, once a year for three years. Between attacks she was very nervous, the hands jerking at times. In the past six weeks the condition had become exaggerated and she had lost 15 pounds. Examination showed marked choreiform movements and large diseased tonsils and adenoids. May 24, 1913, tonsils and adenoids removed. A letter, July 30, 1914, fourteen months after operation, stated her general condition to be very much improved. She had gained 11 pounds and was able to attend school regularly. There was no return of the shaking or jerking. Although this patient had suffered almost constantly for three years with acute exacerbations yearly, yet as soon as the diseased tonsils were removed she commenced to improve, having no recurrence of the trouble.

CASE 3 (88003).—R. A. Boy, aged thirteen, was examined July, 1913. He had had attacks of tonsillitis and enlarged glands for five or six years. Three months previous to examination he had had severe tonsillitis followed by rheumatism of the ankles and knees. He was not confined to his bed, but was unable to walk. Ten days before examination he became very nervous; his left arm and leg commenced to jerk and his shoulders to shrug.

At examination the patient was thin and pale, with typical and fairly marked choreiform movements, especially of the left arm and leg. There were enlargement of the heart and mitral regurgitation; the tonsils were enlarged and diseased; the adenoids were large. July, 1913, his tonsils and adenoids were removed. A letter one year later stated that the boy developed typhoid fever one week after operation, but his rheumatism and chorea subsided, and as soon as he had recovered from the typhoid his general condition markedly improved. There had been no return of his rheumatism or chorea. The fact deserves emphasis that the chorea subsided in this case, notwithstanding his typhoid infection.

CASE 4 (93876).—E. L. Girl, aged seventeen, was examined October, 1913. She had had inflammatory rheumatism at the age of three, and tonsillitis two or three times every year since. For the past two months she had been very nervous. Her hands were continually jerking and her face twitching. At examination she was pale and anemic; her hemoglobin was 38, and she had fairly marked choreic movements of hands and face. Her tonsils were large and diseased. Tonsils and adenoids were removed October 18, 1913. Information received February 11, 1914, i. e., four months later, stated that the chorea subsided three weeks after operation. She was not so easily excited or tired and her general condition had greatly improved.

CASE 5 (97996).—G. A. Girl, aged five, was examined December 31, 1913. She had had a severe cold five weeks before, and for the past two weeks had not used her right arm. Her right ankle showed a tendency to double under. For several days she had been very restless, hands jerking and tongue protruding. Examination showed the child to be pale and thin, with slight choreic movements of the hands and face, and the right arm used less than the left. There was some mitral regurgitation. Her very large and diseased tonsils were removed January 3, 1914. A letter dated July 30, 1914, i. e., five and one-half months later, stated her general health to be improved, that the chorea had subsided a very few days after operation, and there were no signs of return. Occasionally she complained of a slight pain in the joints.

CASE 6 (97152).—M. C. Girl, aged ten, was examined December 15, 1913. A history was given of indefinite pain in the joints, a severe attack of chorea two years before, and inability to walk for two and one-half months. This attack lasted eight

months altogether, with a less severe recurrence ten months later, lasting only two weeks.   The present attack commenced four months ago, gradually getting worse.   At examination the child was suffering from marked choreic movements, very large tonsils with crypts, and very large adenoids.   Her tonsils and adenoids were removed December 4, 1913.   A letter dated July 30, 1914, *i. e.*, seven and one-half months later, showed that the symptoms subsided immediately after operation.   She had had slight pain in the joints on two or three occasions.   Her nervousness had almost disappeared, and she was rapidly gaining in weight.   This case presented the most marked symptoms of any in our series at the time of operation, yet, as far as can be ascertained from the mother, the symptoms almost immediately subsided.

CASE 7 (103597).—S. B.   Girl, aged ten, was examined April 3, 1914.   She had always been a nervous child, and since having typhoid fever three years before her nervousness had increased. Examination showed the child well nourished, very restless, with tonsils large and diseased and medium-sized adenoids.   A diagnosis of chorea was made.   On April 9, 1914, tonsils and adenoids were removed.   Upon examination May 28, 1914, her restlessness and nervousness seemed very greatly improved.   The diagnosis was somewhat doubtful in this case.   The tonsils were removed on general principles, chiefly on account of their size and diseased condition.   The results of the operation were not as definite as in the other cases.

On grouping these cases I find that four gave a previous history of inflammatory rheumatism and six of tonsillitis.   The three giving no inflammatory rheumatism history had had tonsillitis, and the one, with no history of tonsillitis, had had inflammatory rheumatism, so that all gave a history either of inflammatory rheumatism or of tonsillitis, or of both.

Duration.—Two had frequent spells for three years; one for two years; the remaining four had only one attack, from which they were still suffering at the time of examination.   This attack had been present four months in one case, two months in two cases, and two weeks in each of the remaining two.   All presented choreiform movements at the time of operation.

The severity of the symptoms was marked in five cases; six

had very large diseased tonsils; one had medium-sized tonsils with crypts.

Cardiac Complications.—Four had mitral regurgitation; three had no cardiac lesion.

These children were usually very anemic, languid, and in a delicate state of health. When their tonsils were removed not only did their general health improve, but the choreic movements ceased in a remarkably short time and did not return. In a very few weeks they were in a different condition both mentally and physically. Such favorable and uniformly good results are very encouraging, and the facts produced are at least strong circumstantial evidence that diseased tonsils, in the majority of cases, are the primary cause of chorea, and that, when the focus of infection is removed during an acute attack, the symptoms very soon subside.

SUMMARY

1. It is important to make a careful examination of the upper air-passages in nervous children.

2. The close relationship between chorea and the rheumatic infections is seen from clinical observations and, more recently, from bacteriologic investigations.

3. Diseased tonsils are frequently associated with chorea and should be dealt with in its treatment.

4. Rapid cessation of choreic symptoms has occurred in the writer's experience after tonsillectomy during the acute stage.

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2. Wilson, G.: "Treatment of the Portal of Entry of Systemic Diseases," New York Med. Jour., 1911, xciv, 765.
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SURGERY OF THE TONSIL*

JUSTUS MATTHEWS

Since the normal function of the faucial tonsil has not yet been discovered, we can base our indications for surgical procedure only on known pathologic facts and clinical results observed in similar cases. The mere fact that enlarged tonsils exist should not be considered as evidence of a pathologic condition unless they produce either local or general symptoms. Large tonsils may mechanically cause symptoms by obstruction of respiration or deglutition or by interference with speech.

Tonsils of large size or high position may exert pressure on the Eustachian tubes, causing earache, tinnitus, or deafness, or favoring suppurative disease of the middle ear and mastoid. The crypts may furnish sites of accumulation of decomposing materials or growths of fungus which may cause irritation or produce disagreeable odors.

The presence of a new-growth, either benign or malignant, is rare; but when it does occur, it is a positive indication for early and complete removal of the tonsil.

Tonsillitis, acute or chronic, and peritonsillar abscess are the local symptoms most frequently requiring relief. Patients as well as physicians recognize that these conditions and symptoms call for surgical interference which, in the great majority of instances, means tonsillectomy, since other procedures have few, if any, advantages and many disadvantages.

Recently a great deal of attention has been given to the foci of infection which are the causes of such systemic or localized

affections as arthritis, synovitis, endocarditis, anemia, urticaria, neuroses, and various other functional disturbances. These foci have been found in the teeth, the nasal sinuses, the gastro-intestinal tract, and other regions, but in the tonsils more often than in all others combined. It is in cases with these more grave conditions that the medical man to-day is most frequently and urgently advising the removal of tonsils. Since any portion of tonsillar tissue large enough to inclose a crypt may harbor an infective process capable of scattering virus through the system, it has become apparent from experience that, especially in these cases, a complete removal of the tonsils is imperative to insure dependable results.

It is sometimes asserted still that tonsillectomy involves a greater liability to injury of the throat, sepsis, and hemorrhage than does tonsillotomy. Injuries to the throat can be the result only of inexpert or careless operating, and rarely occur except during the early experience of those attempting an operation the technic of which they have not acquired. Post-operative sepsis is more apt to arise in the stump left by tonsillotomy than in the open wound of a tonsillectomy. In the experience of all the men whose opinions I have obtained hemorrhage has been more frequent, more severe, and less readily controlled after partial than after complete removal of the tonsils. This disposes of the question as to whether tonsillectomy or tonsillotomy should be the operation of choice, and leaves the latter to be chosen only when the technical skill of the operator does not warrant him in attempting the former. The cardinal requirements of an operation for tonsillectomy are the complete removal of the tonsil with its capsule, the preservation of the peritonsillar tissue in as nearly normal a condition as possible, and the avoidance of risk to the patient. Secondary considerations are that the operation should be done as quickly and as painlessly as consistent with the former requirements.

The tonsil is operated on more frequently than any other organ of the body. There is little doubt that more of these operations are performed by those ill prepared to undertake them than is the case with any other operation. The observations of a great

number of post-operative results from all parts of this country and abroad have demonstrated that but a small fraction of patients examined have had both tonsils completely removed without injury to the surrounding tissues. The histories of these cases indicate that a large percentage of them have failed to obtain relief from their original complaints, and not a few have lost rather than gained by the operation. This is remarked not to deter any one from performing operations on the tonsils, but to call attention to the usual deficiencies and to urge that those who do perform these operations shall take their responsibilities not too lightly, but have a proper ideal of the desired results and endeavor to acquire a technic necessary to attain such results.

Tonsillectomy should be recognized as a major operation in its difficulties of technic and in the importance of the consequences of success or failure. Patients should be as thoroughly examined and prepared as for any other major operation. The condition of the heart, lungs, and kidneys should be investigated, and a careful history taken to ascertain that sufficient indications for operation exist, and that such indications outweigh any possible contraindications. The history of hemophilia should be considered, though there is little doubt that it is a condition more rare than the number of fatalities attributed to it might lead one to suppose. In case of doubt, the coagulation time of the blood should be taken.

The choice of anesthetic depends upon the experience of the operator and upon the operative procedure employed, as well as the age and condition of the patient. The same care should be exercised before the use of local anesthesia as before the use of general, but it should be recognized that patients sustain operation under local anesthesia better and experience less disturbance and discomfort during and after operation if a full meal has been taken within a few hours before operation.

The practice of forcibly holding children while operating without an anesthetic has fortunately fallen into disuse. The struggles of the patient and the haste of the operator often resulted in such traumatism to the structures of the throat as to cause serious de-

formities, while the fright and shock to many victims remained for
years, sometimes interfering seriously with subsequent examina-
tions or treatments.

In the use of some types of operation general anesthesia is al-
ways necessary, but with other types local anesthesia may be em-
ployed. Ethyl chlorid and gas possess the advantage of being the
easiest general anesthetics to take, and the latter is safe, but both
give so short a period of anesthesia as sometimes to hasten or pre-
vent completion of the operation. Chloroform has often been
said to be a safe anesthetic, especially for short operations on
children, but a study of the statistics of fatalities from chloroform
anesthesia shows a considerable number of deaths. Therefore,
many believe that the administration of chloroform is rarely, if
ever, justifiable.

Ether administered by the open-air drop method gives a fairly
quick and satisfactory anesthesia. Also, there are many devices
for the administration of ether and the drainage of the operative
field, some of which prove of great help to those accustomed to
their use. Therefore, when all things are considered, it is probable
that ether is still the best and safest general anesthetic.

In an experience covering several thousand cases operated on
under local anesthesia in the Mayo Clinic we have found novocain
to be the most satisfactory local anesthetic. It gives a more uni-
form anesthesia than quinin or cocain, and apparently is less liable
to cause local or general bad effects. It may be used freely in
solution of 0.5 to 2 per cent., with very rarely signs of toxic effects,
giving a practically complete anesthesia in most cases, and always
a sufficient degree of anesthesia to permit a successful completion
of the operation. A syringe with an extension and curved needle
is used, and from one to two drams are injected into the fascial
space between the capsule and the surrounding muscles. The
operation is commenced from three to five minutes after the in-
jection.

There are many methods of operation which, when skilfully
performed, fill all requirements, and with but little choice between
them. It is, therefore, most important that the operator choose

the one which appeals most to him and perfect himself in its use.

During the last few years the Sluder tonsillectome and Sluder's method of using it for completely removing the tonsil have been taken up by many operators, especially in Europe. This method has numerous advantages, especially that of simplicity, and in the hands of some men gives a high percentage of perfect results; but the observation of the work of many men, some of them of great skill, has demonstrated that there is more or less frequent failure to remove all the tonsillar tissues and that this failure is most liable to occur in those septic cases of scarred, flat, or very soft tonsils which most urgently require a complete operation. Hemorrhage is said to be frequent and severe following the use of the tonsillectome. The operation requires general anesthesia, which is often inconvenient and sometimes positively contraindicated.

Various types of dissection operations, either complete or supplemented by the use of the snare, have been favored by many. The use of the finger for enucleation of the tonsil is a method no doubt capable of development to a high degree of efficiency, but possesses the disadvantages of requiring a general anesthetic in all cases and involves a liability to more or less serious traumatism of the structure of the pharynx by bruising or rupture of the muscles.

The various methods of sharp dissection avoid to a great extent this danger, but carry with them increased danger of hemorrhage. Dissection by a semi-sharp knife, as described below, combines many of the good features of each method, and lessens the liability to unfavorable results. The instruments used are the Robertson curved knife, the Richards forceps, the Tiding snare, a tongue-depressor, and occasionally curved scissors.

After anesthetization by novocain as described, the tongue-depressor is placed well back on the tongue and the base of the tongue drawn forward until the edge of the palatoglossus muscle is sharply defined. In the angle between this and the lower pole of the tonsil is the point at which the fascial plane between the capsule and muscle can be most easily found. The point of the

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knife is inserted at this place, and swept upward along the poster-
ior surface of the muscle, which separates easily and smoothly
from the capsule. At the upper pole of the tonsil care must be
taken not to cut too high into the velum palati. At this point the
knife is given a turn and a pull downward to free the upper pole
from its attachments, which are usually slight, and then swept
downward between the capsule and posterior pillar. The upper
pole of the tonsil is then grasped with the blades of the forceps on
the faucial and capsular surfaces, and drawn from its fossa down-
ward and toward the midline, where it is held firmly. The knife
is then used with a pushing motion to separate the muscles from
the capsule from above downward, taking care not to rupture or
separate the fibers of the muscles or fasciæ. When this has pro-
ceeded as far as the insertion of the superior constrictor muscle,
the motion should be in the direction of its fibers so as to separate
them smoothly from the capsule and not from the underlying
tissues.

After this has been accomplished and the tonsil remains at-
tached only by its lingual prolongation to the tissues below the
lower pole, the snare is passed over the forceps and tonsil, tight-
ened, and pulled back against the lower pole. The pull of the
forceps is then relaxed as the snare is closed. This causes the
wire to cut cleanly between the muscles and tonsillar tissues with-
out loss or traumatism to either.

This method of operation takes from forty seconds to three
minutes, is usually nearly or quite painless, and is attended by but
slight hemorrhage. It is applicable to all types and conditions
of tonsils irrespective of shape, size, or consistence. When ad-
hesions or scars of peritonsillar abscesses or of previous operations
exist, it is sometimes necessary to make use of the curved scissors,
but usually it is sufficient to draw the edge of the knife across the
more resisting tissues after the softer ones have been pushed away.

Primary hemorrhage varies from a few drops to a few ounces,
and in only a small number of cases has it been necessary to take
measures to check it in order to complete the operation im-
mediately, or to send the patient from the office within a few

moments. This is to be accounted for by the fact that the only vessels severed are those that enter the tonsil, and these are torn apart at their point of entering the capsule, where they are never large and where they most readily retract and close of themselves. The larger vessels in the muscles and fasciæ are never opened, as they are pushed back with the tissues in which they lie by the flat surface of the knife.

Early secondary hemorrhage occurs in about 2 per cent. of cases and is very rarely severe. In my experience it has never required anything but the application of a hemostat when the bleeding point was visible, or the packing of the tonsillar fossa with gauze when the bleeding point could not be located.

Violent exertion, hot drinks, and the use of a gargle should be avoided during the first three hours, as they predispose to hemorrhage. Late secondary hemorrhages occur in only a small fraction of 1 per cent., and are rarely of consequence, as the bleeding is usually a capillary oozing and easily controlled by simple means.

As results of proper tonsil operations we may expect complete relief of local symptoms, and often the cure of general diseases or symptoms caused by reflexes or infections arising in the tonsils.

HOUR-GLASS STOMACH AND DUODENUM *

GEORGE B. EUSTERMAN

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Hour-glass deformity of the stomach is sufficiently infrequent always to be of interest to the clinician. In our experience the condition has occurred in 6 per cent. of the cases of chronic gastric ulcers and in 0.5 per cent. of the cases of duodenal ulcers. Although the literature on the former is extensive and case reports are numerous, only a few of the latter cases have come under observation. In the material herewith presented only the organic permanent types of cases are considered and classified according to whether the condition followed chronic benign ulcer, carcinoma, or lues.

ETIOLOGY

The great majority of hour-glass stomachs are largely the result of an intrinsic ulcerative process. In a few instances the deformity results from post-operative adhesions following excision of a gastric ulcer, compression by an extrinsic tumor, congenital bands, or fistulas. The ingestion of corrosives, spasm of the gastric musculature, and tight lacing are minor causative factors in the production of hour-glass stomach. At an earlier period the congenital origin of most cases had many warm supporters. Many theories were held, all perhaps based on insufficient evidence. Even Sandifort's more recent classic report of an hour-glass stomach in a fetus, which on first evidence seemed strongly to support a congenital origin, is inconclusive, since there is undoubtedly such a condition as fetal ulcer, shown in the report of a case by Godhart[1] in an infant which died thirty hours after birth of hemorrhage from

a gastric ulcer. It would be better to speak of the anomaly as intra-uterine or extra-uterine acquired hour-glass stomach. Veyrassat's[2] exhaustive review of hour-glass stomach deals instructively with this phase of the subject. In the opinion of surgeons of the widest experience the theory of a purely congenital origin of hour-glass stomach is strongly disputed. They hold that,

Fig. 1.—(23008.) Ulcer lesser curvature, pars media, which has perforated into liver, forming a small pocket and hour-glass stomach. There was a large residue in the stomach and a small one in the pocket at the end of six hours (Carman).

if the carefully preserved specimens of the museums were properly incised and examined, the provocative ulcer would be revealed in most cases.

SYMPTOMATOLOGY

There is no characteristic symptom-complex. The symptoms are those of peptic ulcer plus obstruction, chief among which are epigastric pain occurring some time after taking food, vomiting,

and loss of weight.   In a few instances in which the upper loculus
was very small and the constriction situated high on the lesser cur-
vature, the symptoms have simulated those of spasm or obstruc-
tion at the cardiac orifice.   Variations in the clinical picture, as in
ulcer or carcinoma of the stomach, depend upon the location and
extent of the lesion and upon the presence or absence and degree

Fig. 2.—(24631.) Perforated ulcer on lesser curvature. Pocket formation in liver. Hour-
glass stomach; constricted area rough and irregular and about two and one-half or three inches in
length.   There was a six-hour residue in the pocket and lower segment (Carman).

of complicating factors, such as perforation, stenosis, perigastric
adhesions, and coincident disease in other organs.

DIAGNOSIS

The diagnosis must be made on the history, laboratory tests,
inflation of the stomach, and by the Roentgen ray.   Occasionally
the passage of the stomach-tube gives the first clue to the condi-

tion present, in those cases in which obstruction is encountered after passing beyond the cardia. This suspicion is increased if retention products are recovered or if the larger portion of lavage water fails to return. The results of test-meal analyses show no characteristic alteration in the chemistry of the stomach—the acid values may be high, low, normal, or an acidity plus lactic acid be present.

Characteristic signs which may singly or in association be present are:

1. Disappearance of fluid introduced through the stomach-tube "as though it had flowed through a hole" (Wölfler).

2. After cleansing of the stomach by lavage a sudden gush of putrid, sour, ill-digested food, etc. (Wölfler).

3. "Paradoxic dilatation," succussion splash in the pyloric cavity after siphonage of the cardiac loculus (Jaworski).

4. Distention of the cardiac loculus, its gradual subsidence, and concomitantly the distention of the pyloric loculus (von Eiselsberg).

5. During this period a gurgling, forcing sound heard over or near the middle of the stomach (von Eiselsberg).

6. On distention with carbon dioxid a large increase, even to a doubling, in the thoracic area, tympanitic on percussion and with a slight distention, clearly demarcated, of the pyloric loculus (Moynihan).

7. Rarely a sulcus may be seen on inflating with carbon dioxid (Schmidt-Monard).

Roentgen Examination

With the development and increasing accuracy in the interpretation of the findings of the fluoroscopic screen and radiographic bismuth plate and their routine application, the above methods are only of historic interest. These special tests, however, may be tried, as some authorities have been able thus to diagnose as high as 50 per cent. of their hour-glass cases. But the Roentgen examination is indispensable, and in our experience has invariably given the first definite evidence of the condition present.

To the clinician, and especially to the surgeon, the term "hour-glass" signifies the biloculation of the stomach by an organic con-striction. Carman[3] states that to the roentenologist the word has less specific meaning, being applied not only to organic, but also to functional, conditions, thus including every stomach which has a bilocular appearance. The functional or spasmodic hour-glass, due to a reflex spasm of the musculature, may exactly sim-ulate the hour-glass of ulcer. As a rule, such a spasmodic in-

Fig. 3.—(94543.) Ulcer lesser curvature at incisura angularis. Contact ulcer on posterior wall, adherent to liver and pancreas. In the directly anteroposterior view no hour-glass is seen, while in the extremely oblique view a broad, rather deep, wave-like, irregular incisura (hour-glass) is visible. There was no six-hour residue (Carman).

cisura and apparent organic hour-glass subsides under the in-fluence of belladonna. Carman further states that, "on the screen and plate such a stomach, whether due to an incisura or the result of adhesions and contractions from a perforating ulcer, shows def-inite division into two chambers with a short canal joining them, the canal being usually near the lesser curvature, thus giving the stomach a B shape. However, one or two cases have been seen

with a pocket in which the canal joining the loculi of the hour-glass was long and rather centrally placed."

"The organic hour-glass of carcinoma is occasioned by the projection of a tumor-mass into the gastric lumen or by infiltration and contraction, as in scirrhous carcinoma. The hour-glass

Fig. 4.—(100277.)   Spasmodic hour-glass stomach which persisted in spite of palpation. No antispasmodic given.   x-Ray diagnosis: "Probable ulcer, high on lesser curvature."   At operation, an ulcer of the duodenum the size of the head of a lead-pencil was found on the anterior wall just below pylorus.   The case illustrates the danger of overconfidence and the necessity of taking every precaution to eliminate spasmodic conditions simulating organic lesions (Carman).

of carcinoma usually shows characteristic irregular filling defects. The canal uniting the chambers is generally longer than that seen with ulcer, and often has a median situation in the gastric axis, resulting in an X shape."

Kretschmer[4] emphasizes the following points bearing on the

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Kretschmer[4] emphasizes the following points bearing on the

differential diagnostic characteristics of malignant and benign hour-glass:

1. That in malignancy the division between the loculi consists of a horizontal and a vertical band, while in the benign it is a more or less horizontal constriction.

2. It is characteristic in hour-glass stomach that the lower loculus is filled by the upper emptying into it, whereas in malignancy both portions fill equally. The hour-glass form caused by the presence of a tumor extrinsic to the stomach is usually determinable by the smoothness and regularity of the projecting mass and by its behavior to palpatory shifting during the screen examination.

STATISTICAL REVIEW (1907–1913 INCLUSIVE)

In our series there were 37 cases of hour-glass stomach the result of benign gastric ulcers; of these, 24 were females and 13 males. The ages ranged from twenty-five to seventy years. The average age was forty-five years; average duration of symptoms, nine years. Twenty-two, or 65 per cent., were operated on during the third and fourth decades of life. The symptom-complex was typical of peptic ulcer in 80 per cent. A small percentage of error in diagnosis was shown in the cases which perforated and simulated cholelithiasis, and in the markedly obstructed cases, with tumor, cachexia, and achlorhydria which simulated gastric carcinoma. Pain, variable in degree, was a symptom common to all the cases. In the cases which perforated (16) it was acute and often prostrating; in 15 instances it was definitely localized to the left epigastrium. General epigastric and posterior radiation was common. Tenderness was present at some time in all the cases, and in 70 per cent. while under observation. In 27 (65 per cent.) there was a definite onset of pain from one-half to four hours after taking food; in 13 of these the onset was from one-half to one and one-half hours after food. In the remaining 11 the pain was noted two to four hours after meals; in 7, not stated; and in 5, irregular. Relief of pain by food, soda, or vomiting, or by combination of these measures, was noted in 95 per cent. Hyperacidity and vom-

iting were present in 70 per cent. of the cases; hematemesis, single or repeated, in 13 (35 per cent.); associated melena in 9 (24 per cent.). There was definite gross obstruction after twelve hours, and altered blood in the gastric extract was present in 35 per cent. of the cases. The average total acidity was 47 per cent., free hydrochloric acid, 36 per cent., acid salts, 12 per cent., and achlorhydria in 7 cases.

Fig. 5.—(24551.) Organic hour-glass stomach with constriction high up. Slight obstruction at cardia. No residue after six hours. Note that constriction is concentric, which is quite characteristic of carcinoma, resulting in an X shape as contrasted with the eccentric B-shaped hour-glass of ulcer. Carcinoma found upon exploration (Carman).

PATHOLOGY

Calloused saddle ulcers of the lesser curvature, often extensive and adherent to the liver, with variable degrees of inflammation and constriction, were noted in 57 per cent. of the cases. The site of the ulcer in the remainder was as follows: Prepyloric and lesser curvature, 4; posterior wall and lesser curvature, 6; fundus and greater curvature, 2; posterior wall, 4. It will be noted that the lesser curvature, in which over two-thirds of the gastric ulcers are situated, was the site of involvement in 31 out of 37 cases

(84 per cent.).   Chronic or subacute perforation was present in
16, with resulting perigastric adhesions and implication of the
liver or pancreas, or both.   The ulceration was frequently ex-
tensive, involving all the coats.   Crater formation or sloughing of a
calloused ulcer was marked in 3 instances.   The ulcers of the
posterior wall were all of the perforating or penetrating type in-
volving the pancreas.   In these the posterior wall was shortened,

Fig. 6.—(24352.)   Ulcer on posterior wall near greater curvature.   Hour-glass stomach.   Small
residue after six hours (Carman).

the greater curvature was drawn up into the mass, and the hour-
glass deformity resulted.

The favorite site of constriction in our cases was at the pars
cardiaca or media; the upper loculus was usually the smaller,
owing to the high situation or extent of the ulcer.   There was
coincident ulcer of the duodenum with pyloric stenosis in seven
cases.

In an earlier surgical experience with six cases Moynihan[5] especially noted: (1) Perigastric adhesions, the result of a perforating ulcer with the formation of a thick cord running downward from the liver and sharply pressing in the anterior wall-space of the stomach; (2) ulcer with local perforation and anchoring to the abdominal wall; (3) circular ulcer with subsequent cicatricial contraction and induration. This condition may follow chronic simple ulcer, but the hour-glass would be incomplete.

Fig. 7.—(97022.)   Large ulcer on posterior wall of stomach, with deep crater size of a twenty-five-cent piece.   High hour-glass.   Small residue at the end of six hours (Carman).

Spannaus[6] reported 34 cases of hour-glass stomach. In this series an ulcer located on the lesser curvature and posterior wall was the most common etiologic factor. In the greater number the constriction was in the form of a ring, the stomach being freely movable and without clinical symptoms of ulcer. In the lesser number the ulcer was seen as a flat, hard area about the size of a dollar, and the stomach was adherent to the posterior wall and the pancreas. At times the ulcer represented a tumor formation.

MALIGNANT HOUR-GLASS

There were 8 of these cases noted in our clinic within the past seven years—7 males and 1 female. The average age was 53.5 years; average duration of symptoms, two years. Obstruction was present in one-half the cases; altered blood and Oppler-Boas bacilli in the gastric extract in all. The acid values might have

Fig. 8.—(19843.) Ulcer on posterior wall six inches above pylorus; many adhesions. Hour-glass stomach. Crater of ulcer size of a nickel. The lower pouch comprises about two-thirds of the stomach; the upper pouch, about one-third. Large residue after six hours (Carman).

been misleading had it not been for the advanced age of the patient, the short duration of definite symptoms, and the marked cachexia or tumor or both. Achlorhydria was noted three times; the average total acidity was 25; free hydrochloric acid, 13; and combined acids, 12. A huge carcinomatous ulcer was the causative lesion in 5 cases and a malignant tumor in 3. All were

situated in the lesser curvature, and in 3 the posterior wall was involved.

LUETIC HOUR-GLASS

In this group there were 3 cases—2 males and 1 female, ages twenty-four, twenty-six, and forty-one, respectively. A history of definite infection was obtainable in all. Active specific treatment had been previously carried out without amelioration of the gastric disturbance. The average duration of symptoms was three and two-thirds years. Obstruction obtained in one case. The acid values were similar to those of gastric cancer. The findings are briefly:

CASE 1.—Hour-glass constriction at the juncture of the fundus and antrum. Large irregular ulceration on anterior wall. Several ulcerations and thickening along greater and lesser curvatures to esophageal opening. The ulcers were multiple. Operation: gastroplasty followed by gastrostomy.

CASE 2.—The stomach small and adherent. Strictured at three points—cardia, antrum, and pylorus. Liver and spleen considerably enlarged, soft, and mottled. Numerous adhesions about the liver. Operation: dilatation of the esophagus; gastrogastrostomy for median and pyloroplasty for distal stricture.

CASE 3.—Ruffled stomach; multiple ulcers in the posterior wall extending to cardia. Peculiar appearance of pyloric end and body of the stomach. Stomach narrowed to the size of an adult wrist. Operation: Witzel jejunostomy.

MISCELLANEOUS

One case, a female of twenty-nine who had had symptoms for more than twelve years, was the result of a congenital fistula with a lumen the size of a lead-pencil running as a band from the lesser curvature two inches above the pylorus to the lesser curvature two inches below the cardiac orifice. The channel was excised and both ends closed by a purse-string suture. In another case the hour-glass constriction was the result of post-operative adhesions. There had been two operations elsewhere on the gall-bladder and

stomach. Operation: Undoing the anterior gastro-enterostomy and separation of adhesions.

Hour-glass Duodenum

There were 8 cases in this series: 6 males and 2 females. With 2 exceptions the duration of symptoms ranged from ten to thirty-eight. The typical symptom-complex was present in all the cases. With one exception pain appeared two to four hours after

Fig. 9.—Hour-glass duodenum (Mayo).

meals and was regularly relieved by food, soda, or lavage. Hematemesis and melena were noted in 3 instances. Marked pyloric obstruction was present in all but one case. The acid values were high. The preoperative diagnosis in 7 of the 8 cases was that of duodenal ulcer with pyloric obstruction.

Pathology

The ulcers in these cases are large, thick, calloused, and sometimes with crater formation. They may be extensive and usually implicate the pylorus. The posterior or anterior superior walls are invariably involved, the ulcer extending downward from the upper aspect of the pylorus on the superior wall of the duodenum, producing a pouching like an hour-glass. This pouch may be $1\frac{1}{2}$ to 2 inches in extent. Extensive contraction of the upper

surface just below the pylorus and again 2 inches below this had in one instance formed a cicatricial canal 1½ inches in length, with very marked obstruction, forming an hour-glass duodenum for 2 inches.   In one instance the ulcer apparently began at the pylorus.   The duodenal ulcer was large and thick.   The cicatrix continued on the superior surface, encircling the duodenum at two different points one inch apart, thus producing the hour-glass type.
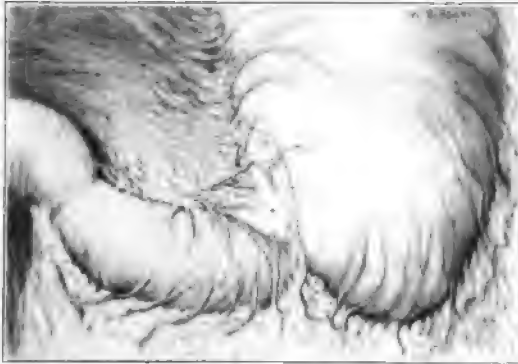
Fig. 10.—Hour-glass stomach.   Dotted lines show proposed resection (Mayo).

The stomach was markedly hypertrophied or dilated, owing to the obstruction.

TREATMENT

The treatment is essentially surgical, otherwise the prognosis will be unfavorable.   In a large majority of cases of hour-glass contractions of the stomach and of the duodenum continuous symptoms of a marked obstructive and painful nature had been noted for a number of months prior to the operation, and the progressive decline made surgical interference imperative and welcome to the patient.   The nature of the operation depends on the existing condition.   The versatility of the operator with respect to gastric surgery is best exemplified in these types of cases.   In cases of hour-glass stomach gastrogastrostomy is a desirable operation, although resection in continuity, when it can be done, has

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given good results. In some cases, however, gastrojejunostomy fulfils the indications admirably.[7]

In our first group (37 cases) the operations were as follows: Gastrogastrostomy, 10; posterior gastro-enterostomy, 8; resection in continuity, 2; partial resection, 1; Witzel jejunostomy, 1; exploration, 1; anterior gastro-enterostomy, 1; Hartman gastroplasty, 5; combined operations: gastrogastrostomy and gastro-
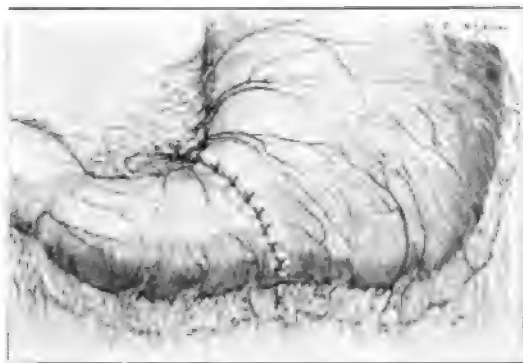
Fig. 11.—Result of resection of the obstructing ulcer in hour-glass stomach (Mayo).

enterostomy, 3; gastroplasty with excision, 2; anterior gastro-enterostomy with excision, 1; gastroplasty and gastro-enterostomy, 2. In the malignant hour-glass cases a palliative gastro-enterostomy or exploration only was done. In the 8 cases of hour-glass of the duodenum posterior gastro-enterostomy was done in 7 and excision with plastic enlargement in 1.

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CHRONIC GASTRIC DISTURBANCES: DIFFERENTIAL DIAGNOSIS *

GEORGE B. EUSTERMAN

The subject of differential diagnosis of chronic gastric disturb-
ances is a broad one, covering, as it does, very many of the problems
of internal medicine.   However, I shall be as brief as is consistent,
dealing largely with that type of gastric disturbance of a chronic,
recurrent, and painful or distressing nature, and resistant to ordi-
nary methods of treatment; and, at the same time, emphasizing
some of the features of the symptomatology and laboratory find-
ings, which in our experience are of greatest practicable diagnostic
value.

Under the term *dyspepsia* we may have a broad classification;
and successful treatment of the condition presupposes a proper
diagnosis of the factor or factors underlying the complaint.   Is
the condition a functional one, dependent upon some inconsistency
of eating, environment, or habit, or upon some acquired or in-
herent nervous instability?   Is it the result of some lesion of the
stomach itself, or of contiguous organs associated with the stom-
ach in the digestion and preparation of food for assimilation?

Chronic simple ulcers of the stomach and duodenum have a
fairly definite symptomatology.   They furnish the typical syn-
drome of dyspepsia.   The complaint is a chronic one.   The at-
tacks or spells alternate with free intervals, as a rule, and last from
several weeks to a month or longer.   During such a spell there is a
daily repetition of the trouble, which is characterized by epigastric
pain and distress appearing at a stated interval after food.   This

pain or distress, or both, is entirely or partially relieved by any measure which may dilute, neutralize, or remove the hyperacid gastric secretion. The disease has a tendency to become progressively more severe, the exacerbations becoming more frequent and longer in duration, and the pain less easily or less completely controlled. At any time during the course of the disease hemorrhage or symptoms of perforation may supervene. When pyloric stenosis with dilatation and stagnation occurs, the whole picture is intensified. Then there are more or less continuous symptoms of pain coming on less regularly after meals, accompanied by increased flatulency, regurgitation, nausea, and vomiting of retained gastric contents. If obstruction is partial or intermittent, the symptoms are modified. A carefully developed history, dating back to the inception of the trouble, is important. In these cases it is also well to remember that it is not so much the degree or location of the pain as it is the time when the pain appears and the manner in which it is relieved. Pain is noted in 95 per cent. of all cases, and is the most constant symptom. Chronicity, with periods of exacerbation and remission, was present in 85 per cent. of the cases in our series. Food relieved the pain, gas, and acidity in 76 per cent.

The symptoms are less variable with duodenal than with gastric ulcers. Spring and fall seizures are quite common in the former. "Hunger pains," so called, are frequently absent. Definite hemorrhage occurs in less than one-third of all cases. Tenderness plays a minor rôle, as this symptom is invariably absent until the peritoneum is involved. Persistent tenderness, from a considerable to a marked degree, suggests protected perforation. In the majority of instances one may make a reasonably safe clinical diagnosis of ulcer, but to say that a given case is definitely gastric or duodenal is a more difficult matter. In atypical cases or in types in which there is a paucity of symptoms, the result of test-meal analyses and roentgenoscopic findings are of correspondingly greater importance.

In the differential diagnosis the clinician must always remember that gastric disturbances dependent on irritations in the gall-

bladder or appendix may so closely, although with less regularity, simulate the symptom-complex of ulcer as to make uncertain a conclusive diagnosis in a small percentage of cases, even when taken in conjunction with complete laboratory data.

The question is frequently asked, "Can you clinically differentiate between gastric and duodenal ulcer?" This may be done with a fair degree of certainty in clear-cut types. Uncomplicated ulcers of the duodenum and pylorus are usually so definite in their symptomatology that they may be diagnosed with but little trouble. Yet frequently in cases of calloused saddle ulcers of the lesser curvature the symptoms are typical of the duodenal syndrome; while, on the other hand, a duodenal ulcer at times is more characteristic of the gastric type, i. e., the pain may come soon after food, the location and radiation of pain may be well to the left, etc.

In ulcer of the stomach proper the attacks are not so clear cut as in the duodenal and pyloric types, nor are the day-by-day symptoms so clearly defined. In cases with lesions well above the pylorus the symptoms are apt to be continuous for longer periods, or remission, rather than free intervals, is apt to be present. The pain and distress are not so often eased by food; or small amounts of food may give relief, while increased food may give distress. More care in diet and careful attention to the physical and nervous states are necessary. Soda relieves when food does not. Pain begins earlier, as a rule, often disappearing before the next meal, and thus the food-relief feature is minimized. But pain in from one-half to one hour after food is the usual rule, and is of great diagnostic significance. Radiation and diffuseness of pain are considerably more extensive in the gastric than in the duodenal types. In addition, vomiting is rather more common in gastric ulcers than in uncomplicated ulcers of the duodenum and pylorus. Owing to a delayed emptying capacity, the vomitus usually contains food in an early to a moderate stage of digestion. Hematemesis is more frequent in cases of the gastric type.

In disease of the gall-bladder the typical hepatic colic is easily recognized, and when it is followed by jaundice, there is hardly

room for doubt. In cases of early perforating peptic ulcers the painful seizures are frequently mistaken for hepatic colic and require special care in diagnosis. When there has been an antecedent history suggestive of ulcer the proper interpretation is less difficult. When there is nothing else to guide one, careful analysis of the detailed features of an attack is helpful. Careful inquiry is made into the mode of the onset, the location, character, severity, and duration of pain, and also the measures found to control it. On the other hand, the presence of diaphragmatic spasm, upward pressure, posterior radiation, and sudden cessation are characteristic of biliary colic. Absence of spasm, severe continued penetrating pain, and rigidity of the upper abdomen, with leukocytosis, are more suggestive of a perforative seizure.

In gall-bladder disturbances there are dyspeptic symptoms of various degrees:

1. Light attacks of distress, gas, and upward pressure, coming soon after food or at irregular times, and often of sudden onset and short duration, and eased by belching or perhaps by slight vomiting or regurgitation. These symptoms may pass away almost unnoticed and without treatment, though various measures may get credit for a natural return to health.

2. A more pronounced type in which the affection in the gall-bladder is chronically advanced, perhaps with duct obstruction and infection, and in which a history of colic with fever or chills may be remote or entirely absent. In such types there obtain periods of irregular frequency and duration in which there is a daily complaint of flatulency, distress, epigastric pain, sour, bitter regurgitations and eructations, all associated more or less with the taking of food.

3. The ulcer type, which very closely simulates the second type in some respects. These conditions are more difficult to differentiate from peptic ulcer.

The strawberry gall-bladder is often an offender. Perversion of the gastric secretion and pyloric spasm, often reaching their climax at some definite time after taking food, may give rise to symptoms usually associated with peptic ulcer. What the actual

underlying factors are is not yet definitely proved, but it appears reasonable to presume that infected bile causes disturbances of the pancreatic secretion. Pyloric spasm may be produced by derangement of the balance of the alkalinity of the neutralizing secretions.[1] In about 10 per cent. of all duodenal and gastric ulcers there was coincident disease of the gall-bladder operatively demonstrated. This fact obviously gives rise to difficulties in diagnosis.

It is of the greatest importance to the patient to recognize the possibility of a reflex cause for dyspepsia. Such cases frequently are assiduously and scientifically treated for peptic ulcer. Improvement under such treatment is of a very temporary nature, and a proper surgical procedure is the only guarantee of permanent relief.

Chronic recurrent types of appendicitis may closely simulate the clinical picture of a peptic ulcer, owing to reflex motor and secretory perversion of the gastric functions. This possibility should always be borne in mind, especially when dealing with persistent dyspepsias of younger individuals. A definite history of appendiceal colic or localized tenderness at "McBurney's point" is often entirely absent. This is also true of adults in whom an attack of appendicitis is remote or entirely forgotten, and the relation of their present or recurring gastric disturbance is not recognized or associated with the preëxisting lesion. It must not be lost sight of that the diseased appendix may give rise to subsequent pathologic changes in the gall-bladder, stomach, and duodenum.

Graham[2] has tersely stated that, "In those diseases which oftenest cloud the diagnosis, such as chronic cholelithiasis and chronic appendicitis, we obtain our greatest diagnostic aid from the wide irregularity of symptoms during the period of attack. Yesterday's pain came before meals, to-day's pain after meals, to-morrow's pain an 'all-day miserable feeling.' Food-ease yesterday because fasting the previous day; to-day food-pain wholly reflex; vomiting one day and gas another; yesterday well, to-day in the depths mentally. Nothing follows in sequence day by day because the stomach behaves properly unless irritated by the distant

lesion, and this extrinsic lesion is irregular in its influence. The stomach then delivers what symptoms it may when the irritation is great enough."

Gastric cancer may be classified under two main clinical types:

1. That in which the antecedent history is definite or fairly regular for the accepted symptom-complex of peptic ulcer, but the lesion at the time of examination and operation has undergone malignant degenerative changes. This type constitutes above 60 per cent. of all our cases of cancer. Clinical recognition of such changes may be quite impossible, for in early stages the evidence is entirely microscopic, yet conclusive.

2. That type of so-called "primary" cancer beginning usually in the fourth to sixth decades of life, and in which a previous history of gastric disturbances is entirely or practically absent. Whatever the type, when cancer has once gained a foothold, the well-recognized symptom-complex is manifest in all cases.

Then there are bizarre types of gastric cancer or cases obscured by a neurosis which may remain unrecognized except for routine gastric analysis and roentgenoscopic examinations, the results of which furnished the first suspicion of malignancy. Gastric disturbances and secretory changes, associated with cachexia the result of a serious constitutional disease of the heart, kidneys, lungs, liver, or blood, often give rise to considerable difficulty in the differential diagnosis clinically.

One is impressed with the many extraneous conditions that may cause gastric disturbances. Obviously their recognition is of the greatest importance, especially when operative interference is being considered. Among these are migrain, locomotor ataxia, Pott's disease, syphilis, thoracic or abdominal aneurysm, cardiospasm, angina, myocardial insufficiency, herpes zoster, lead-poisoning, pneumonia, and nephritis. Chronic pancreatitis, with or without jaundice, and usually secondary to gall-bladder disease, is a frequent and often unrecognized cause of "stomach trouble." The treatment is essentially surgical.

Splanchnoptosis, with its train of gastric, intestinal, and nervous disturbance, is of timely importance and interest. We

are inclined to conservatism in the surgical treatment of such cases at present.

Test-meal Analysis.—Laboratory methods have their limitations. The more the findings of the laboratory are confirmatory of the clinical symptoms, the greater is their diagnostic import. Examination of the gastric contents should be routinely done, as the results furnish a link in the chain of evidence, and often prove of invaluable aid in obscure cases. The passage of the tube alone and the nature of the contents withdrawn may throw the first light on the presence of a stenosed, strictured, or spastic condition of the cardiac or pyloric orifices. Air-inflation gives some idea of the size, mobility, and position of the stomach and of pain and tender areas during distention. Occasionally a mass, not in evidence under ordinary conditions, is readily palpable during this procedure. High acid values and hypersecretion suggest the presence of a benign ulcer. Not infrequently the acidity may be normal, and yet an ulcer may be operatively demonstrated. In 48 per cent. of our cancer series free HCl was noted, although in reduced amount. The absence of free HCl, in addition to the Oppler-Boas bacilli, indicates cancer in over 90 per cent. of cases. If, in addition, altered blood, sarcinæ, and tumor are present, the diagnosis of a malignant neoplasm is the logical conclusion.

Too much dependence must not be placed upon the presence or absence of occult blood in the gastric extract or meat-free stool. Persistent occult blood in the stool is characteristic of gastric cancer or bleeding ulcer. We employ only the simple methods of chemical and microscopic examination following the Ewald test-break fast.

Roentgen-ray Examination.—This procedure, in experienced hands, is of invaluable diagnostic aid. The field is comparatively new, but large; great progress is being made, and many points of dispute will be settled in the near future. In my experience the Roentgen ray so far has been most helpful in cases of gastric cancer, not only in demonstrating the lesion, but in giving accurate information as to its location, extent, and operability.

As regards ulcer of the stomach: Definite diagnosis is made in

over 60 per cent. of the cases by a combined use of the fluoroscope and roentgenogram of the bismuth-filled stomach. This is easily the most important technic in the localization of the lesion. According to Carman,[3] the signs that are cardinal and more or less pathognomonic are: (a) Visualization of the bismuth-filled crater of a callous ulcer; (b) the accessory cavity of a perforating ulcer; (c) the incisura. There are other signs not determinative, but suggestive, of ulcer, the details of which are not necessary to state here.

In duodenal ulcer the cardinal sign is that of heightened peristaltic activity of the stomach, and definite diagnosis may be made radiologically in about 50 per cent. of all cases. In these cases, however, the clinical symptom-complex is so definite in about 90 per cent. that the present Roentgen-ray limitations are of less significance. In addition, the radiographic examination may give the first definite evidence of spasmodic or hour-glass deformity, cirrhosis, and of other malformations, whether due to intragastric or extragastric disease-processes. The screen also furnishes most reliable information as to the position, size, tonus, mobility, peristaltic activity, and emptying capacity of the stomach.

Proper correlation of the clinical and physical findings with laboratory and roentgenoscopic data, bearing in mind the possibility of reflex conditions which so often simulate true organic lesions in every aspect, will make for a safe diagnostic conclusion in most cases. In any circumstance we should not forget the need of the patient, who is chiefly concerned in seeking relief for his suffering. It is often sufficient to conclude that a lesion is present, regardless of its exact nature or localization, and to determine the patient's needs as to treatment in the light of the manifest symptoms.

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FUNDAMENTAL CONSIDERATIONS IN THE DIFFERENTIATION OF GASTRIC NEUROSIS FROM ORGANIC ABDOMINAL DISEASE *

HERBERT Z. GIFFIN

In a day of the aggressive development of surgery clinical diagnosis must know more definitely its reason for any show of conservatism. An improper conservatism has often conserved the disease rather than the patient. Every history of gastric disorder may mean the incipiency of some serious organic disease, and all the burden of careful observation falls on the physician when he arrives at a decision to advise against surgical treatment. A mistake of this character assumes its most striking and serious proportions when a carcinoma of the stomach has been tentatively diagnosed as gastric neurosis.

On the other hand,—and it is this aspect of the subject that I wish to emphasize,—much needless and often harmful surgical treatment has been carried out on patients who were very plainly neurasthenic in constitution. Those observers who have had a large experience in nervous diseases have always recognized this fact and have never countenanced it. Meanwhile many of these very specialists in nervous diseases have been so ultraconservative with regard to the recognition of gastric and duodenal ulcer and those reflex types of indigestion caused by disease of the gall-bladder and appendix that some surgeons have been made bold as a consequence. There have been those on both sides, however, who, by reason of an especial sanity, have maintained the mean position. They have realized the harmful consequences to medical

and surgical progress that would follow because of mistaken
diagnoses and misdirected treatment; for whatever is harmful to
medical and surgical progress as a whole is harmful to the good of
the greatest number.

With regard to malignancy, it has been learned that the un-
successful attempt to lengthen the life of an individual a few months
by some surgical procedure may lead several of his neighbors to
delay during a curable stage; in view of this fact even the success-
ful attempt to lengthen life may at times not be justifiable. It has
not, however, been sufficiently appreciated that a neurasthenic
individual who complains more after operation than he did before
may prejudice literally hundreds against what might be to them a
beneficent treatment.

It is therefore essential that the greatest care be exercised in
differentiating gastric neuroses from organic surgical diseases.
With this there will also result a greater efficiency in recognizing
the truly surgical conditions, so that some serious affection may be
even less likely to be overlooked.

In connection with the diagnosis of gastric neurosis certain
fundamental considerations are essential—considerations which
it may be of interest to classify and discuss.

The first of these has to do with the distribution and physiology
of the sympathetic and the craniosacral autonomic systems.[1, 2]
Fibers from the autonomic system are distributed to the eye,
throat, heart, lungs, stomach, intestines, and other abdominal
viscera and the genital organs. This distribution accounts for
the symptomatology in a great many instances. Peculiar throat
complaints, salivation, hot flushes, palpitation, cardiac distress,
a variety of abdominal symptoms, pelvic hypersensitiveness, and
anal spasm, in addition to all those features which make up the
picture of a general neurosis, are consequently associated with
gastric symptoms. In those patients with symptoms of indiges-
tion, hypersensitiveness, and instability of the cerebrospinal ner-
vous system and variations in the tonus of the autonomic sys-
tem may, in fact, clear the diagnosis. It is the rarest incident to
obtain a clear-cut history of gastric disorder which can be properly

diagnosed as gastric neurosis without evidences also of a more general neurosis. It is quite generally recognized that a majority of the cases of neurasthenia are of the congenital asthenic type;[3, 4] consequently the family history and the entire personal history of the patient must be considered as a whole in the diagnostic consideration of a given case.

The second consideration which may be of assistance in the diagnosis of these cases has to do with the distinction between a functional disorder and a neurosis.[5] It is remembered that the irregular functional type of indigestion need not be secondary to a neurosis. Hypersecretion, hypermotility, pylorospasm, and gastrospasm are functional disorders but may not be due to a neurosis. Indigestion associated with tuberculosis, anemia, nephritis, or cirrhosis of the liver is functional, but not neurotic. The vomiting associated with brain tumor is a reflex vomiting, and may be regarded as functional, but not neurotic. Consequently it would seem to be a safer plan in connection with the diagnosis of a given case to regard an indigestion which presents those irregular symptoms commonly considered as of the functional type as a secondary indigestion, and then to proceed by elimination to demonstrate that it is secondary only to a neurosis.

The third consideration would emphasize the importance of variability in the diagnosis of abdominal neuroses. By this is meant both variability in the story that the patient tells, a variability in the patient's story from day to day and a variability in the symptoms from time to time. In a case of gastric neurosis it is a rare incident to obtain a history of recurring indigestion which maintains a constant type of symptoms. The gastric neuroses so commonly described as either sensory, motor, or secretory in character are seen from a practical standpoint to be possible of no such classification. There is always a combination of these types of disorders. When a constant type is approached, one's suspicions of organic disease are always aroused. It was long held that but one type of gastric neurosis gave a constantly recurring picture and that was the type supposed to be associated with hyperchlorhydria. But the degree of acidity is a variable

finding, and we now know that the recurring history of burning pain, sour eructations, and relief from soda, once regarded as often due to a simple hyperchlorhydria, practically always means ulcer or some type of organic reflex disorder secondary to an abdominal lesion. Consequently the only remaining constant type has been eliminated, and variability assumes even greater importance in the diagnosis of abdominal neuroses.

By way of comparison of this question of variability allow me to review the more constant types of organic abdominal disease. In a study of all the cases of gastric and duodenal ulcer that were operated on in the Mayo Clinic between 1906 and 1911 inclusive (a total of 816 cases) Graham[6] arrives at many valuable conclusions. Chief of these is the evidence concerning periodicity, pain, and pain relief. Pain or severe gnawing distress was noted in 95 per cent. of the cases, relief of pain by food in 76 per cent., while a periodicity in the attacks of indigestion with intermissions over a term of years occurred in 85 per cent. of the cases. That is, a periodicity of attacks of indigestion with intervals of freedom extending over a number of years is almost constant in the duodenal and pyloric types of ulcer before complications are too far advanced. Consider in addition to this the characteristics of the indigestion, in which pain and very sour regurgitation come regularly at a certain interval after food, with more or less relief from food or alkalis, and the diagnosis of ulcer, save in the exceptional case, is seen to be much simplified. Moreover the symptoms assume a constant type. Compare this with the variability of gastric neurosis in respect to periodicity, pain and pain relief, and the distinction is not difficult save in a small percentage of instances. Hunger-pain with food-relief almost never occurs in gastric neurosis. Conversely if there be no history of hunger-pain the probability of duodenal ulcer being present is small.

In ulcer of the stomach proper there is a certain degree of irregularity which does not occur in duodenal ulcer. The symptoms are apt to be continuous for longer periods, remissions rather than free intervals occur, pain may begin soon after meals, often from one-half to one hour, and may disappear before the next

meal; relief from taking food is consequently of shorter duration. Even here, however, there are definite pain and usually sour regurgitation, and these will ordinarily distinguish the condition from gastric neurosis in which the patient may give other evidences of an unstable nervous system and is much more apt to complain of heaviness, fullness, abdominal pulsation, nausea, and bitter eructations, foul taste, and coated tongue. In fact, it may be stated here that the very bad condition of the mouth and tongue, with their foulness, fissures, and deposits, are much more commonly seen in connection with neurotic conditions than in ulcer and cancer, and suggest the possibility of a chemical basis for the disorder.

Again difficulty is encountered in the differentiation from gastric neurosis of those types of indigestion due to chronic colicless gall-bladder disease and chronic appendicitis without acute exacerbations. Here there is apt to be a wide irregularity of symptoms; the time of pain with relation to food intake is likely to vary from day to day. Food ease may come one day and not the next. The attacks are not clear-cut, because the symptoms are dependent on the behavior of a distant lesion. Some of the cases, however, will give a history which cannot be distinguished from that of ulcer, but the extreme variability of neurasthenia is generally lacking. There is also an absence of neuralgias, headache, palpitation, pelvic hypersensitiveness, weakness, and easy tiring.

It is whenever any of these lesions, that is, gastric or duodenal ulcer, gall-bladder disease, or appendiceal disease, occur in a congenitally neurasthenic individual that the greatest difficulty of all is encountered. The fact can never be lost sight of that a patient with neurasthenia may also have a definite organic lesion. Consequently one may not yield to the temptation of too quickly concluding that a patient is neurotic only. Fortunately in most of the cases of this type two definite histories stand out prominently, one the neurotic picture and the other the picture of the organic disease present. That is, the history can be divided rather sharply into two distinct groups of symptoms. In other instances the symptoms of organic disease rather strangely relegate the neu-

rotic symptoms to the background. "I used to be nervous, but
these pains are different and much worse than my former ones"
is the usual story.

It would appear then that the most important considerations
leading to a diagnosis of gastric neurosis are: (1) The existence of
extreme variations in the type and course of the indigestion; (2)
the elimination of definite evidence of a lesion which might cause
a reflex functional type of indigestion; and (3) the presence of
symptoms pointing to an unstable or hypersensitive nervous sys-
tem.

A fourth and very important consideration in a study of indefi-
nite types of abdominal disease is that of the findings upon ex-
amination of the gastro-intestinal tract by the Roentgen ray.
The diagnostic value of the Roentgen ray in the cases which came
to operation during 1913 in the Mayo Clinic was 93 per cent. for
carcinoma of the stomach, 83 per cent. for gastric ulcer, and 50
per cent. for duodenal ulcer. These statistics, of course, could
not include a reckoning on those cases which never came to opera-
tion. One can quite safely conclude, however, that the findings
upon fluoroscopic examination of the gastro-intestinal tract are
already demonstrated to be of very definite assistance, providing
such examinations have been carried out by an experienced op-
erator in a fearless manner.

The diagnosis of duodenal ulcer is usually quite definite upon
a review of the clinical history only. The history of cancer, on
the other hand, may be mistaken for a functional type of indiges-
tion and may even be considered to be secondary to a neurosis. In
cancer, however, the chronicity of the present complaint is usually
lacking, there is a short history of a new and different character,
and Roentgen examination gives a large measure of assistance.
The practical value of the Roentgen examination is more con-
spicuous, however, in the differentiation of ulcer of the stomach
proper, because here one obtains an irregular history, frequently
suggesting a reflex, functional, or a neurotic type of indigestion,
and in these patients there is, as a diagnostic aid, an 83 per cent.
value in the Roentgen examination as based on cases coming to
operation.

The mental attitude of the patient, if properly analyzed, is an aid to correct diagnosis in cases of abdominal neurosis.   There is a tone of despair in his complaints; he would rather die than exist as he is; there is a wide fluctuation in his sense of well-being; he is up one day and down the next; he is keen for an excessive amount of work at one time and mentally inert at another.   There would almost seem to be some temporary cerebral abnormality as well as an affection of the lower centers.   There probably is a certain degree of psychoneurosis with every neurasthenia.

Chronic starvation often completes the vicious circle in cases of gastric neurosis.   These patients have no appetite, and, if they eat, they either vomit immediately or the food lies so heavily and causes such a feeling of fullness and bloating that the condition is to them intolerable.   This may be partly due to the congenital visceroptosis that is often an anatomic attribute of the congenitally neurasthenic individual.   It is undoubtedly also due to a hypersensitiveness of the stomach.   From a therapeutic standpoint the recognition of chronic starvation is of the greatest importance, because if ulcer be diagnosed by mistake, the patient may either be operated upon or dieted unnecessarily, when in reality he is suffering from neurasthenia plus the effect of starvation.   Forced feeding brings about improvement in the general condition and consequently effects a more or less complete disappearance of the gastric symptoms.

STATISTICAL *

The evidence in corroboration of one's opinion concerning the diagnosis of gastric neurosis comes from the acceptance of, first, the experience of those physicians who have had most to do with a study of nervous diseases; second, the experience of surgeons with patients who have been operated on in different clinics from one even to a dozen times without improvement, often with positive harm; and, third, the fact that large numbers of patients with the accepted symptoms of abdominal neurosis have never developed organic disease.

* I am indebted to Ethan Flagg Butler for assistance in reviewing case histories.

'14—4

It may be of interest to review in this connection in a general way a group of statistics bearing on this subject from the files of the Mayo Clinic. During the year 1913, 58 resections were done for carcinoma of the stomach. In this group there were two patients who gave histories which might have been mistaken for gastric neurosis. These patients presented a very irregular symptomatology extending over a period of years and blurred by the description of many vague and bizarre complaints. Fortunately, the fluoroscopic examinations prevented error. In one instance the Roentgen examination disclosed a filling defect in the pars pylorica, and in the other case a moderate pyloric obstruction was demonstrated. During the year 1913 we have been able to find one case in which, while a tentative diagnosis of gastric neurosis was made, the patient developed carcinoma of the stomach.

In a review of 100 cases in which gall-stones were removed at operation 14 histories showed a neurotic tinge. These are of two groups: First, the majority, which gave both a clear-cut history of neurosis and in addition a clear-cut history of gall-bladder disease; second, those in which the symptoms were irregular and confusing. In these it is noteworthy that in the type of indigestion the complaints of an excessive formation of gas and the eructation of large amounts of gas were most prominent and that upon physical examination there were localized tenderness and rigidity in contradistinction to that general abdominal hypersensitiveness so commonly observed in abdominal neuroses.

In a series of 1000 consecutive recent cases of neurasthenia in which a prominent gastric symptomatology was presented, we found that 199 had been previously operated upon, some of them in our clinic, in an attempt to relieve these symptoms and that although there may have been a pathologic lesion present at the time of operation, no relief of their principal complaints had resulted. Of these 199 patients, 175 had had one operation, 16 had had two operations, 7 had had three operations, and one had had four operations.

These operations were chiefly upon the appendix, the pelvic organs, and the gall-bladder.

Patients who had 1 operation—175

Appendectomies (negative exploration, 37) (no exploration, 63).. 100
Operations on pelvic organs (chiefly on the ovaries)........... 50
Operations on stomach.................................... 6
Operations on gall-bladder................................ 11
Operations on kidney (chiefly for movable kidney)............ 5
Miscellaneous... 3

It is beyond the scope of this paper to discuss these findings in detail. It may be stated, however, that the evidences of a general neurosis were so prominent and the signs of local disease so indefinite that these cases have been classed as neurasthenia.

Patients who had 2 operations—16

Primary operation, appendectomy......................... 13
Primary operation, pelvic................................ 2
Primary operation, gall-bladder.......................... 1

The subsequent operations in these cases were for adhesions, painful scar, oöphorectomy, visceroptosis, drainage of the gall-bladder, etc.

Patients who had 3 operations—7

In this group there was a considerable variety in the types of the operations. In 2 cases the operations were entirely upon the stomach; in 5, on the gall-bladder, appendix, kidney, pelvis, and for adhesions.

One patient who had 4 operations

First, movable kidney; second, gastro-enterostomy; third, "entero-anastomosis" and oöphorectomy; fourth, gastro-enterostomy undone and appendectomy.

In addition to these 175, 28 of the 1000 patients had been formerly advised to have an operation for the relief of symptoms which seemed to be so definitely neurotic in their character that surgical treatment seemed to us to be contraindicated.

It would appear in the above tables that the most numerous offenses are committed upon patients with symptoms localized in the region of the appendix.

CONCLUSIONS

It is the common experience of large surgical clinics that too many patients suffering from various types of abdominal and pelvic neuroses have been advised to undergo surgical treatment, and the greatest number of mistakes is apparently made in connection with those cases in which the diagnosis and prognosis should not be difficult. On the other hand, most searching examinations are often required in cases which, at the first examination, appear to be neurotic in order to avoid the occasional mistake of not recognizing an abdominal lesion.

Cases of gastric neurosis demand a very general kind of consideration. Important general factors which enter into this consideration are—(1) The analysis and grouping of those symptoms referable to hypersensitiveness and instability of the nervous system; (2) the careful exclusion of those diseases which, in a reflex manner, so commonly produce an indigestion of the functional type; (3) the realization that variability, both in the story that the patient tells and in the symptoms from time to time, is most important; (4) the application of the Roentgen findings; (5) the recognition of certain psychic elements, and (6) a review of all these data in the light of the personal and family history of the patient.

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THE ROENTGEN DIAGNOSIS OF GASTRIC ULCER *

RUSSELL D. CARMAN

The value of the Roentgen ray as a diagnostic aid in gastric ulcer has in my opinion been greatly underestimated. Until recently I shared the orthodox belief that only a moderate percentage of ulcers of the stomach could thus be demonstrated, but the diagnostic percentage herein quoted has convinced me that the Roentgen ray has no apologies to offer in this line.

Last September, in a paper before the Indiana State Medical Association, I ventured the statement that the Roentgen ray was perhaps worth 65 per cent. in the diagnosis of gastric ulcer, and that this percentage would probably be materially increased in the future. In confirmation of this I may say that from September 1st to March 1st, 1983 patients were examined at the Mayo Clinic by the Roentgen ray for gastro-intestinal lesions. At operation 47 of this number were found to have gastric ulcer, and 39 of the 47 were diagnosed as such upon radiologic signs, thus giving the Roentgen method a value of 83 per cent. Duodenal ulcers, which are regarded by some as gastric, are not here included.†

I have heard clinicians remark that the Roentgen ray is of considerable help in carcinoma of the stomach, but of little aid in ulcer. In my opinion the relative value is the reverse, so far as the clinician is concerned. In carcinoma he often finds a palpable tumor, food remnants, Oppler-Boas bacilli, and evidences of obstruction as diagnostic aids. In ulcer he has little else than the anamnesis to guide him, which is notoriously uncertain. Hence any method that will give concrete data in ulcer is of distinct value. For the surgeon, on the other hand, the Roentgen ray not only in-

creases the percentage of correct diagnoses of cancer, but also furnishes some information as to resectability and the prospective operative requirements. The diagnosis of ulcer is further important from the fact that an ulcer often shows carcinomatous cells, and its diagnosis is therefore in many instances equivalent to an early diagnosis of carcinoma, at a time when surgery can be the first instead of the last resort.


Figs. 12 X and 12 Y.—(00803.) Two illustrations, X and Y. X is a stereoscopic view of the removed specimen, showing the ulcer at a. Y is a photomicrograph, magnified 4 diameters, of a cross-section through the ulcer. Note that destruction extends down to musculature but not into it. This excavation is the niche seen at a in roentgenogram.

TECHNIC

The lack of a uniform technic for gastro-intestinal examinations is perhaps accountable for some diversity of opinion among radiographers. In England an effort is now being made to standardize methods, and the endeavor will meet with general approval. Whether the movement succeeds or not it is highly important that
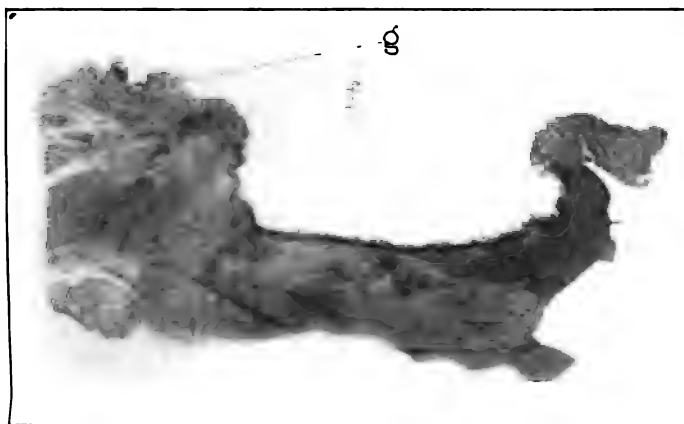
See legend, Figs. 12 X and 12 Y. *f*, Ulcer base, *g*, intact mucosa.

Fig. 12 Z.—(96805.)   Callous ulcer on lesser curvature, posterior wall.   Contact ulcer size of a lead-pencil on anterior wall.   Posterior ulcer deeply calloused and recently perforated, covered with thick mat of adhesions.   While two ulcers were present, only the one on the lesser curvature, posterior wall, gave radiologic signs, as here shown.   *a*, Niche; *b*, incisura.   No six-hour residue.

the individual operator have a rather steadfast routine in order to give him a constant basis for comparison.

Our technic* may be defined as the combined fluoroscopic and skiagraphic examination with the double opaque meal. Barium sulphate is used in the six-hour meal, and at the time of examina-

Figs. 13 X, 13 Y, and 13 Z.—(94543.) Ulcer lesser curvature at incisura angularis. Contact ulcer on posterior wall, adherent to liver and pancreas. Three views are shown—X, Y, and Z. In X, directly anteroposterior, no definite signs are seen. Y is a moderately oblique view, showing irregular indentation of greater curvature at *b*. Z, extremely oblique view, showing crater of ulcer at *a* and more pronounced incisura at *b*. The wave-like, irregular incisura is the result of the multiple ulcers. All three plates, X, Y, and Z, were made at one sitting in rapid succession. Stereoscopic view of specimen shown in Fig. 13 W.

tion the patient is given bismuth subcarbonate in water, followed quickly by bismuth subcarbonate in potato-starch pap.

I am a strong partizan of the screen, and believe that its employment is absolutely requisite to a satisfactory inspection of the digestive tract. So-called "serial radiography" is by no means an

* This may be found in detail in "The Roentgen Ray as an Aid in the Diagnosis of Gastric Cancer and Ulcer," Journal of the Indiana State Medical Association, 1913, vi, 485–505.

efficient substitute, no matter how many plates are made or how much language is devoted to a description of the eccentricities they reveal. The only valid objection to the screen is the possible danger to the operator, but with up-to-date protective apparatus I believe this danger is practically nil.

During the screen examination, which rarely requires more than five minutes, often less, the behavior of the stomach to palpation,

Fig. 13 Y.—See legend, Fig. 13 X.

respiration, and variations of abdominal pressure, its mobility and peristaltic activity, are all carefully observed from different angles. When it is completed, plates are made if desired, with the patient either prone or standing, usually the latter.

As first used, the six-hour meal originally contained bismuth. The six-hour limit for normal gastric evacuation, while arbitrary, was well sustained by experience. Since barium sulphate leaves

the stomach more rapidly than bismuth, a barium residue after six hours is even more significant than a bismuth residue. The employment of the six-hour meal is more convenient both to patient and operator than hourly examinations beginning with the taking of the first meal. It is not very important to know whether the stomach is emptied in two hours or four, but it is necessary to learn whether a liberal time limit for evacuation is exceeded. The

Fig. 13 Z.—See legend, Fig. 13 X.

fluidity of the bismuth water and its small amount favor certain features of the examination, while the bismuth-supporting property of the potato-flour pap and its palatability make it a desirable medium for complete filling.

VARIETIES OF ULCER

As seen at operation, four classes of gastric ulcer may be distinguished: (1) Small, exceedingly shallow, mucous erosions and

slit-like ulcers; (2) penetrating or callous ulcers with relatively deep craters; (3) perforating ulcers with or without accessory cavity-formation, and (4) very early carcinomatous ulcers.

Of these four classes, the first—the small, shallow, mucous erosions — offer the greatest difficulty of roentgenologic detection. They are either superficial denudations or mere slits in the mucosa, incapable of holding enough bismuth to make a visible niche. Unless accompanied by an incisura or a six-hour rest, their presence will hardly be even suspected, much less positively determined.

The penetrating ulcers which have burrowed

Fig. 13 W.—(94543.) Stereoscopic view showing multiple ulcers. Mucous membrane folded irregularly. Ulcers seen at a; healed ulcer at b. Roentgenograms shown in Figs. 13 X, 13 Y, and 13 Z.

more or less deeply into the gastric wall show a definite crater, which may be either quite round, oval, or irregular. The degree
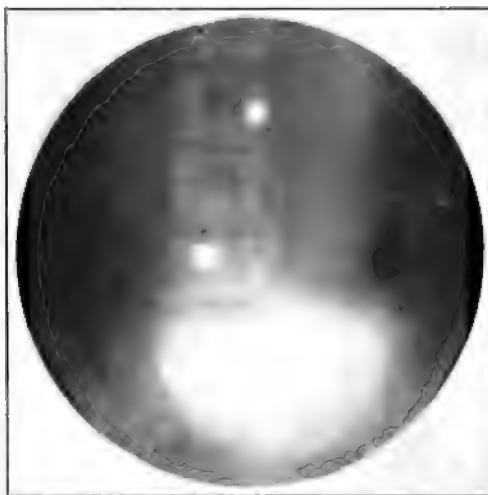
Fig. 14 X.

Figs. 14 X and 14 Y.—(18993.)   Ulcer size of a twenty-five-cent piece high on posterior wall, near lesser curvature, adherent to pancreas.   Two views are shown, X and Y.   X shows incisura at *b*, in the secretion zone; note hypotonicity of stomach.   Y was taken immediately after X, and was made with the patient prone.   It shows the incisura more plainly than in X, illustrating the advantage of the prone position for radiographing high incisuræ in hypotonic stomachs.   The incisura was present at two different examinations, resisted vigorous palpation, and was not affected by an antispasmodic. No niche was seen.

Fig. 14 Y.—See legend, Fig. 14 X.

of facility with which this crater can be seen as a niche by the Roentgen ray depends upon its size and location.

Perforation of an ulcer and a continuation of the destructive process into an adjacent organ or tissue result in the formation of an accessory cavity. Those that I have seen were either in the liver or in the pancreas. None, shown later by operation, failed to be visible on screen and plate. Perforation may, of course,

Fig. 15.—(23248.)   The incisura seen at *b* was produced by a band of adhesions.   No ulcer was present, although diagnosed radiologically as gastric ulcer.   The incisura survived vigorous palpation and antispasmodics, and was present at a second examination.

occur without the production of a pocket. In this event the radiologic signs are like those of callous ulcer, plus, in some instances, the distorting effect of adhesions.

The very early carcinomatous ulcers are not, as a rule, distinguishable macroscopically from non-malignant ulcer. Their roentgenologic signs are not different from those of penetrating or perforating ulcer.

The positive radiologic diagnosis of gastric ulcer can be based only upon the presence of one of two signs, namely: the niche or the accessory pocket.

Other signs which are corroborative but not diagnostic of themselves are: (1) The incisura; (2) hour-glass stomach; (3) residue in the stomach after six hours; (4) lessened mobility; (5) localized pressure-tender point; (6) delayed opening of the pylorus; (7) acute fish-hook form of the stomach with displacement to the left and down; (8) gastric hypotonus, and (9) antiperistalsis.

Fig. 16.—(100277.) Spasmodic hour-glass stomach which persisted in spite of palpation. No antispasmodic was given. x-Ray diagnosis: "Probable ulcer, high on lesser curvature." At operation an ulcer of the duodenum, the size of the head of a lead-pencil, was found on the anterior wall just below the pylorus. The case illustrates the danger of overconfidence and the necessity of taking every precaution to eliminate spasmodic conditions simulating organic lesions.

THE NICHE

The term "niche" I shall apply for convenience to the visualized crater of a callous penetrating ulcer, an excavation wholly within the wall of the stomach.

The niche, which shows as a various-sized, bud-like projection from the contour of the bismuth-filled stomach containing no occluded gas and emptying with the stomach, is the most frequently occurring pathognomonic sign of ulcer. As an ulcer may exist in any part of the stomach, it follows that the niche may also be found anywhere, but those I have seen thus far were either on the lesser curvature, usually above the incisura angularis,

Fig. 17.—(94561.)   Two ulcers of the stomach.   First, a calloused ulcer with a great deal of thickening, ¼ inch above pylorus, on posterior inferior wall.   Second ulcer on lesser curvature, one inch to right of incisura angularis.   Note bulging of stomach at *a*.   Marked prepyloric contraction at *b*, corresponding to the location of the first ulcer.   No six-hour residue.

or on the posterior wall.   As a rule, a niche can be moved about with the gastric wall by palpation.   While the niche is often regularly crescentic in outline, it may sometimes be quite irregular. The size may vary from a mere fleck to a considerable recess.   It is worthy of note that a niche may be demonstrable without extremely deep penetration of the ulcer.   Fig. 12 Y is a photomicrograph of a section through an ulcer in which penetration did not

extend beyond the submucosa, yet the niche was plainly seen as shown in Fig. 12 Z.

When situated upon the vertical portion of the lesser curvature, a niche will usually show plainly in the anteroposterior view. When seated in the pars pylorica, detection is hampered by peristaltic activity and by the difficulty of obtaining any but an antero-

Fig. 18.—(20799.) Large ulcer, lesser curvature, carcinomatous. The carcinomatous condition is indicated radiologically by the large size of the ulcer-crater at *a*. All such cases would, however, be ordinarily diagnosed as ulcer.

posterior view. If located on the posterior wall of the vertical portion of the stomach, an oblique view is necessary to discover it. This view should never be omitted in any examination. Careful observation should be made while the stomach is filling, as a very small niche may be hidden or partially obliterated by gastric distention.

Bismuth in the bulbus duodeni and bowel beyond, adjacent to the stomach's contour, especially the lesser curvature, may super-

ficially imitate a projecting niche, but palpation will readily show the difference.   Distortion by spasm may sometimes, though not often, produce a localized, apparent pouching, resembling a niche. Spasm generally disappears after energetic massage or upon re-examination, but in any strongly suspicious case an antispasmodic should be given.

Fig. 19.—(19835.)   Callous ulcer with niche and incisura.   a, Bismuth-filled crater; b, incisura.

The Accessory Cavity

The accessory cavity, as previously stated, occurs as a result of perforation of the ulcer and an extension of the ulcerative process into adjacent structures, producing an excavation in the tissues outside the stomach.   If situated high up, ulcers of the lesser curvature or anterior wall are apt to perforate against the liver, while those lower down and on the posterior wall may invade the pancreas, forming in either event a distinct cavity.

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I have purposely omitted using the term "diverticulum," generally employed by roentgenologists to describe cavity-formation by perforated ulcers, because in a strict anatomicopathologic sense a diverticulum must have the same lining cells as the organ from which it springs. Inasmuch as an ulcer begins with destruction of these cells, the production of a true diverticulum by an ulcer is hardly possible.

Fig. 20.—(18813.) Ulcer four inches above pylorus on lesser curvature. Crater size of a nickel. *a*, Bismuth filled crater; *b*, slight indentation on greater curvature which was seen moving toward pylorus.

As pointed out by Haudek, the bismuth-filled pocket shows the same fluid and air strata as the stomach. It lies outside of and distinct from the opaque shadow of the stomach.

While usually spheric in outline, the pocket may sometimes be irregularly shaped. Commonly it is immovable by palpation and is tender to pressure, giving a sense of resistance.

Those I have seen ranged in diameter from one to three or four centimeters. A six-hour rest in the stomach is often asso-

ciated with pocket formation. Bismuth often remains in the cavity after the stomach is empty. A recess in the liver moves with respiration, while one in the pancreas does not, and the more anterior situation of the former is shown by an oblique view. Organic hour-glass stomach usually but not invariably accompanies accessory cavity-formation.

Fig. 21.—(95011.) Large callous ulcer, lesser curvature. Bismuth-filled crater easily seen at *a*. No six-hour residue or incisura.

INCISURA

Next in importance to the niche and accessory cavity comes the incisura. Though not pathognomonic, the incisura is perhaps the strongest contributory sign of ulcer. Exploited as one of the earliest practical radiologic indications of ulcer, it has received copious discussion in the literature.

The incisura is an indentation of the gastric wall opposite an

ulcer.   Its production is ordinarily believed to be due to irritation
of an ulcer causing a spastic contraction of the circular muscle-
fibers in the plane of the ulcer.   It may also occur in association
with the scar of a healed ulcer.   Theoretically, it may occur any-
where in the stomach and be seen on either curvature.   Practically,
the vast majority are found on the greater curvature, and most

Fig. 22.—(23147.)   Ulcer posterior wall, perforating into body of pancreas, with a crater the
size of a twenty-five-cent piece.   This is a perforating ulcer without accessory cavity-formation.
Shown to be malignant microscopically.   There was a small six-hour residue in the stomach.   The
bismuth-filled crater may be seen at a.

commonly in the vertical portion of the stomach.   Occasionally
they may be seen in the pars pylorica.

Incisuræ have considerable variation in width and depth.
They may be so deep as almost to bisect the stomach, or so shallow
as merely to dimple the curvature.   This difference in depth is
doubtless sometimes due to the angle of observation.   Each of
two ulcers, even though closely situated, may have its separate

incisura.   The outline of an incisura is commonly sharp and regular, but some irregularity may occasionally be noted.   In one of my cases in which a large, broad, irregular, wave-like incisura occurred in association with a single niche multiple ulcers were found at operation (Fig. 13 Z).

Recognition of an incisura is not difficult, as a rule.   The stomach should be watched during the process of filling; after re-

Fig. 23.—(100795.) Callous ulcer on lesser curvature, four inches above pylorus. Fleck of bismuth at a indicates crater. The amount of bismuth at this point could be increased by manipulating the gastric contents. The diagnosis was based upon the niche as seen during the screen examination. Stereoscopic views of specimen shown in Figs. 24 X and 24 Y.

pletion an incisura may be more or less concealed by overlapping of its borders.   Overlapping may be so marked that gentle pressure may be necessary to visualize the indentation.   The patient should be turned about to permit oblique or lateral inspection of the gastric contour.   An incisura high up in the vertical portion of the stomach may lie wholly in the secretion-zone above the opaque meal and thus escape notice (Fig. 14 X).   Hence the bis-
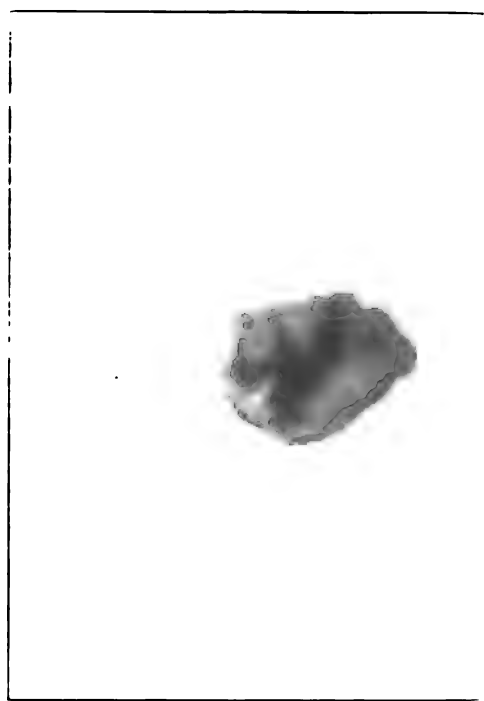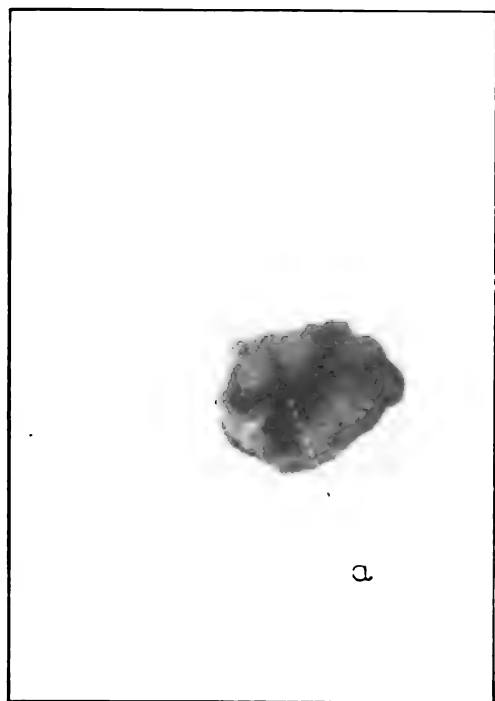
Fig. 24 X.

Figs. 24 X and 24 Y.—(100795.)   Two stereoscopic views, X and Y.   In X note wide-open slit at *a*.   In Y niche seen in cross——
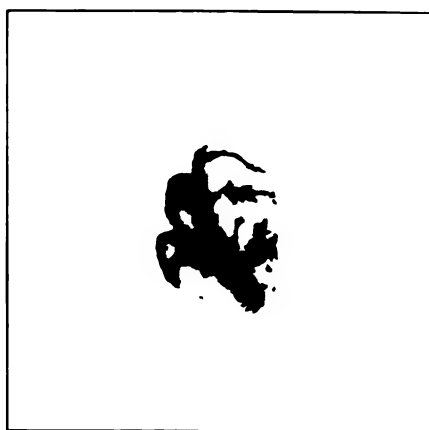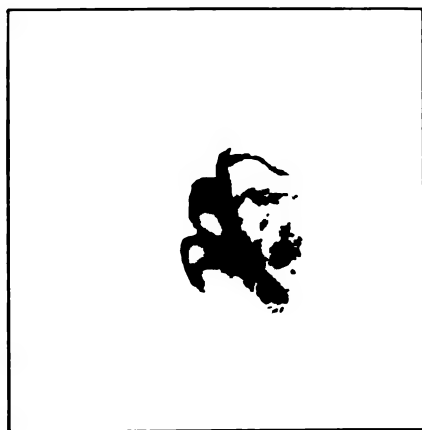Roentgenogram shown in Fig. 23.

Fig. 24 Y.—See legend, Fig. 24 X.

muth should always be forced upward by palpation during screen-

Fig. 25 Y.—See legend, Fig. 25 X.

Figs. 25 X and 25 Y.—(29008.) Ulcer of lesser curvature, pars media, which has perforated into liver, forming a small pocket. Two views are shown, X and Y. In X is seen a small six-hour rest in the pocket at *a*, and large residue in the stomach at *c*. In Y is shown the filled stomach with pocket at *a*, incisura at *b*, and hour-glass constriction. *d*, pylorus; *e*, duodenum.

ing.   To show such an incisura on the plate, radiography in the prone position may be necessary.   In the pars pylorica an in-

cisura is less readily distinguished because of peristalsis. The diaphragm should be actively employed in studying this region.

Fig. 26 Y.—See legend, Fig. 26 X.

Fig. 26 X.—(23106.) Ulcer lesser curvature perforating into pancreas with pocket formation. Two plates, X. and Y, are shown. In X, very small fleck of six-hour residue in pocket at a with strata of secretion and gas above. Large six-hour residue in stomach at c. Y shows filled stomach with accessory pocket a entirely outside shadow of stomach. There was also an ulcer of the duodenum which was not recognized radiologically. This is not surprising, since it is very difficult to show double lesions

True incisuræ must be differentiated from the normal incisura angularis and incisura cardiaca, from the indentation of the greater

curvature where the left costal arch crosses it, from the effect of adhesions, and from spasm. The deep incisura angularis in the angle of the lesser curvature and the shallow incisura cardiaca on the greater curvature are familiar to the roentgenologist. Slightly less familiar is the depression on the greater curvature beneath the left costal arch. Commonly this indentation is broad, shallow, and obviously not a true incisura. However, I have occasionally

Fig. 27.—(94231.) Large perforating ulcer lesser curvature. Niche seen at a. No. 2 six-hour residue. No incisura present.

seen this indentation so narrow and sharp that I was uncertain whether it was a genuine incisura or not. Lifting up the lower pole of the stomach tends to narrow and deepen such an indentation and thus add to the uncertainty. In fact, this sort of manipulation may easily produce an apparent incisura in almost any stomach and should be avoided. Palpatory pressure should be directly backward and not upward if an incisura is being sought for.

An adhesion band may constrict the stomach in such fashion as to simulate an incisura. Fig. 15 illustrates such a case. Small indentations about the pars pylorica due to adhesions from a pericholecystitis are not likely to be mistaken for true incisuræ because of their multiplicity and the accompanying fixation. The most annoying imitations of true incisuræ are those produced by

Fig. 28.—(95948.) Ulcer, posterior wall, lesser curvature; crater size of a penny. Ulcer of duodenum just below pylorus. The ulcer of the stomach was diagnosed on the small niche seen at a. The ulcer of the duodenum was diagnosed on hyperperistalsis, not seen in plate, but present during screen examination.

spasm. The latter often have an appearance and position identical with the former. Their spasmodic character is evident if they move toward the pylorus. Even though stationary, they may be assumed to be spasmodic if they relax and disappear upon vigorous palpation or after the administration of an antispasmodic. The belief is held by some that non-permanent incisuræ may some-

times be caused by small or shallow mucous erosions, but decisive
proof is as yet lacking.

It follows that a true incisura should be subjected to and with-
stand the following tests: (1) It must be constant and stationary;
(2) it must be present when the stomach hangs normally; (3) it
must survive vigorous palpatory manipulation; and (4) it must

Fig. 29.—(19843.)   Ulcer on posterior wall, six inches above pylorus; many adhesions.   Hour-
glass stomach.   Crater size of a nickel.   The lower pouch comprises about two-thirds of the stomach;
the upper pouch, about one-third.   Niche seen at a.   Hour-glass constriction at b.

persist after the patient has been given an antispasmodic to
physiologic effect.

For this latter purpose I am accustomed to prescribe tincture
of belladonna in ten-drop doses, three times daily for two or three
days or until flushing of the skin or disturbed vision indicates
further intolerance.   There is no objection to using atropin

hypodermatically. The screen examination with the opaque meal is then repeated.

The diagnostic value of an incisura which fulfils these conditions depends upon the coincidence of other signs. I would hesitate to base a diagnosis upon an incisura alone. If associated with a niche, as it sometimes is, it assists in confirmation. Less con-

Fig. 30.—(100058.) Perforated ulcer on lesser curvature. Excavation about the size of a five-cent piece adherent to pancreas. Excavation is shown at *a*. Prepyloric irregularity due to adhesions at *b*. Large residue after six hours; no incisura.

vincing but entitled to respectful consideration is the presence of a definite pressure-tender point opposite the incisura, or the association of an incisura with a six-hour residue.

HOUR-GLASS STOMACH

To the surgeon the term "hour-glass" signifies a biloculation of the stomach by an organic constriction. To the roentgenologist the word has less specific meaning, being applied not only to or-

ganic but also to functional conditions, thus including every stomach which has a bilocular appearance, regardless of cause or permanence.

The hour-glass stomach of ulcer may result from—(a) incomplete segmentation by an incisura; or (b) constriction by adhesion bands from a perforating ulcer.

Fig. 31.—(24122.) Large callous ulcer, lesser curvature, posterior wall, high up under liver. Crater of ulcer as large as a nickel. Extensive adhesions to liver and spleen. Residue noted in stomach after six hours. a, Crater; b, incisura.

The hour-glass produced by an incisura may not be found by the surgeon owing to relaxation by the anesthetic. On the screen or plate it shows definite division into two chambers, with a short canal joining them, the canal being usually near the lesser curvature, thus giving the stomach a B shape. This B shape may also be the result of adhesions from a perforating ulcer, with or without pocket-formation. However, I have seen one or two cases

with a pocket in which the canal joining the loculi of the hour-glass was long and rather centrally placed. An hour-glass produced by adhesions will, of course, persist at operation.

The organic hour-glass of carcinoma is occasioned by the pro-

Fig. 32.—(18393.) Ulcer perforated into liver with accessory pocket-formation. Hour-glass stomach. *a*, Upper loculus; *b*, hour-glass constriction; *c*, occluded gas in pocket; *d*, bismuth-filled pocket; *e*, lower loculus. Residue was found after six hours both in pocket and in lower loculus. After the latter was completely emptied the pocket still contained bismuth.

jection of a tumor-mass into the gastric lumen or by infiltration and contraction, as in scirrhous carcinoma. The carcinomatous hour-glass usually shows characteristic irregular filling defects. The canal uniting the chambers is generally longer than that seen

with ulcer, and often has a median situation in the gastric axis, resulting in an X shape.

The hour-glass form caused by the pressure of a tumor extrinsic to the stomach is usually determinable by the smoothness and regularity of the projecting mass and by its behavior to palpatory shifting during the screen examination.

Fig. 33.—(24930.) Large perforating ulcer lesser curvature, size of a silver dollar, adherent to transverse colon and pancreas. Ulcer may be malignant. a, Bismuth-filled crater; b, broad, shallow, irregular incisura. Acute fishhook stomach with displacement to the left and down. No six-hour rest.

Functional or spasmodic hour-glass, due purely to reflex spasm, may exactly simulate the hour-glass of ulcer (Fig. 16). Therefore no hour-glass stomach should be deemed organic until the tests for spasm previously mentioned have been applied. Nor are these tests invariably conclusive, for I have seen a spasmodic incisura and hour-glass persist after belladonna had been given.

Residue

A distinct residue from the six-hour meal, amounting to an eighth or more of the quantity taken, is a relatively common accompaniment of gastric ulcer. Its most common cause is the pylorospasm which frequently accompanies ulcer, but in the

Fig. 34.—(24631.) Perforated ulcer on lesser curvature. Pocket formation in liver. Hourglass stomach; constricted area rough and irregular and about 2½ or 3 inches in length. There was a six-hour residue in the pocket and lower segment.

case of an ulcer at or near the pylorus organic obstruction from scar contraction may be responsible.

A six-hour rest is by no means an exclusive indication of ulcer, since it may occur in any obstructive condition, including carcinoma, duodenal ulcer, and pericholecystic adhesions, as well as reflex spasm from conditions outside the stomach.

LESSENED MOBILITY

More or less fixation often results from perforating ulcer. But fixation may ensue from any perigastric inflammation. Besides, satisfactory determination of the actual mobility of the stomach depends considerably upon its form, tone, and position, and the relative relaxation of the abdominal wall.

Fig. 35 X.

Figs. 35 X and 35 Y.—(96415.) Large indurated ulcer on posterior wall of stomach near lesser curvature, as large as a fifty-cent piece. Many adhesions posteriorly. Two roentgenograms, X and Y, are shown. In X, a direct anteroposterior view, there is seen a slight bulging of the lesser curvature, corresponding to the niche at *a*, and a rather deep, broad, somewhat irregular incisura on the greater curvature at *b*. In Y, an oblique view, the niche is seen more prominently at *a*, while the incisura is shallower, but shows an overhanging upper segment.

TENDER POINT

A sharply localized, pressure-tender point over a niche is of confirmatory value. If limited to an area on the curvature opposite an incisura, but with no niche or accessory pocket existing, suspicion of an ulcer is increased, but a diagnostic opinion should

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be cautiously given.   To be of any value at all, a pressure-tender point must be narrowly circumscribed, as the majority of persons have more or less tenderness in the epigastrium.

DELAYED PYLORIC OPENING

Delayed or scant opening of the pylorus during the period of examination, showing pyloric spasticity or irritability, is not infre-

Fig. 35 X.—See legend, Fig. 35 Y.

quently seen with gastric ulcer.   This sign is of trifling significance, however, as it may occur in numerous other conditions.   Further, a full, free, and early flow through the pylorus may accompany ulcer, as I have noted more than once.

THE ACUTE FISHHOOK

An acutely flexed, fishhook form of the stomach, with displacement to the left and down, noted early as a minor radiologic
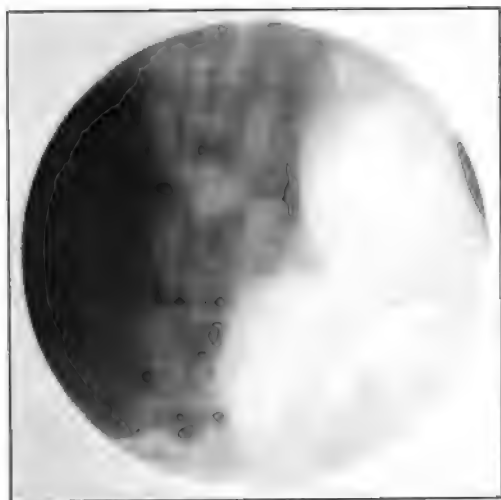
Fig. 36.—(17318.) Small ulcer on lesser curvature, 1½ inches above pylorus. There was a small residue after six hours, and a prepyloric shadow-defect indicating an organic lesion. No incisura. Photograph of the ulcer, shown in Fig. 37, explains the absence of a visible niche.
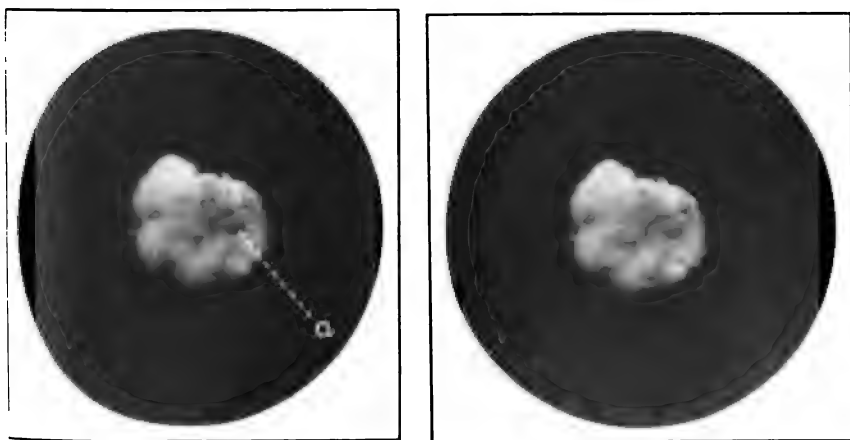
Fig. 37.—(17318.) Stereoscopic view of a slit ulcer, excised specimen. Slit seen at *a*. The character of the ulcer explains the absence of a niche from the roentgenogram shown in Fig. 36.

sign of ulcer, has, I think, received more prominence than it deserves.

The "snail-form" of Haudek (Fig. 17), an extreme degree of flexion due to scar-contraction on the lesser curvature, is of some importance, but corroboration by other signs is necessary to a positive diagnosis.

Fig. 38.—(100081.) Large, indurated gastric ulcer involving the lesser curvature about four inches from pylorus. Crater size of a ten-cent piece. Niche corresponding to crater plainly seen on lesser curvature. More or less hour-glass constriction, mostly spasmodic.

HYPOTONICITY

Gastric hypotonus occurs sufficiently often in conjunction with ulcer to deserve mention, merely, however, as a contributory sign, which is not to be taken too seriously.

ANTIPERISTALSIS

I have thus far seen nothing distinctive in the peristalsis associated with gastric ulcer. Antiperistalsis has been occasionally

noted with ulcer at the pylorus, but this may also be seen now and then with any obstructive organic lesion at or near the pylorus.

ULCER AND CARCINOMA

The roentgenologic signs of ulcer differ so much from those of carcinoma in the vast majority of cases that differentiation requires no effort at all. For example, a callous ulcer with niche

Fig. 39.—(80-200.) Ulcer size of a twenty-five-cent piece, lesser curvature, 1½ inches above pylorus. Considerable induration around the ulcer. There was a No. 2 residue on a scale of four after six hours, with the prepyloric filling defect here seen. Diagnosed radiologically as "lesion at the pylorus."

and incisura, or a perforating ulcer with pocket-formation, has no radiologic resemblance whatever to a well-developed carcinoma, either scirrhous or medullary, and such cases make up the bulk of those patients coming for Roentgen-ray examination. In a general way ulcers always project from the gastric contour, while in carcinoma the growth, with its resultant irregularity,

extends into or encroaches upon the gastric lumen. Between
the typical ulcer and the typical carcinoma, however, there is a
small percentage of cases in which roentgenologic differentiation
is impossible. These are the border-line cases, in which carcinoma
cells are found in the ulcer. In such instances the Roentgen signs
are chiefly those of ulcer, and such a diagnosis is likely to be ren-

Fig. 40.—(101487.)   Ulcer high on lesser curvature.   Hour-glass contraction.   Many adhe-
sions.   The hour-glass stomach persisted after an anti-spasmodic and was present at a second exami-
nation.   Small residue after six hours.   No visible niche.   In this case there was also an ulcer of the
duodenum, not diagnosed.

dered. At operation the nature of the lesion is usually not deter-
minable macroscopically.

Extreme size of an ulcer-crater, as shown by a very large niche,
should make one suspicious of malignancy, a fact which I have
had impressed upon me by experience. A niche three centimeters
or more in diameter is apt to show microscopic signs of carcinoma
(Fig. 18).

Differentiation of pyloric ulcer from pyloric carcinoma is most difficult. Here, in either event, the only radiologic signs may be a six-hour rest and an atypical irregularity of contour, and the roentgenologist can only say with certainty that a lesion exists.

A correlation of his findings with the clinical data may justify an opinion that one or the other condition is present.

As I have repeatedly urged heretofore, this correlation should be made in every case. But I have small patience with clinicians

Fig. 41.—(15614.) Large, callous ulcer, size of a twenty-five-cent piece, involving the lesser curvature, three inches above pylorus. No radiologic signs except a small six-hour residue.

who, using the Roentgen ray because of its spectacular effect, arrive at diagnoses which are 100 per cent. clinical, but give the Roentgen ray credit therefor and thus foster the impression that the Roentgen ray alone will elucidate the most recondite lesions.

VALUE OF SIGN GROUPS

In this analysis I have endeavored to emphasize the niche and the accessory pocket as being the only conclusive signs of ulcer.

Next in order I would place the incisura, the hour-glass stomach. and the six-hour residue. An incisura that has withstood the above-mentioned test, occurring with a six-hour rest in the stomach, is, in the writer's opinion, sufficient evidence upon which to make a radiologic diagnosis of gastric ulcer. This opinion would. however, be greatly strengthened if a second examination furnished the same evidence.

CHRONIC ULCERS OF THE STOMACH AND DUODENUM *

WILLIAM J. MAYO

First Period: 1893 to 1900. Pyloric Obstruction.—The first case of pyloric obstruction in St. Mary's Hospital was operated on in 1893. This operation was a Heineke-Mikulicz pyloroplasty. The second operation was a gastrojejunostomy with the Murphy button. From this time on a gradually increasing number of such operations were performed in our clinic. However, only those cases with marked obstruction at the pyloric end of the stomach were operated on, and at the time of the operation the obstruction was believed to be the result of gastric ulcer, although the exact location of the ulcer, whether in the pyloric end of the stomach or in the duodenum, was not determined.

Second Period: 1900 to 1906. Growth of Knowledge the Result of Surgical Observation.—During this period it was recognized that obstruction was a terminal condition, and a study of the subject was commenced with a view to the earlier termination of a malady which exposed the patient to serious dangers and more or less constant disability and distress. There was much discussion of mucous ulcers, erosions, and a variety of supposed lesions which was not the result of actual observations at the operating table, but of an attempt to furnish a pathologic basis for the symptoms complained of by the patient. This atmosphere of uncertainty gradually disappeared, and patients were explored for symptomatic indications, but not operated on unless a pathologic basis for those symptoms could be demonstrated at the time of the operation.

The Murphy button was gradually abandoned for the suture, and the anterior method of gastrojejunostomy replaced to as great an extent as possible by the posterior.

Third Period: 1906 to 1914. Development and Improvement in Diagnosis.—The great value of the history and physical findings in diagnosis was emphasized. Operative experience showed the relation of the clinical symptoms to the lesion, and the value of the purely laboratory examinations of gastric contents was found to have been overestimated. The Roentgen ray gradually won first place in the diagnosis of these lesions, and the necessity for the excision of gastric ulcers, because of the menace of cancer, was recognized.

Our Present Status.—Up to December 31, 1913, 1841 cases of acute and chronic ulcers of the stomach and duodenum had been operated on in our clinic. Of this number, 437 were females and 1384 were males. The early clinical view of a preponderance of females over males was thus shown to be in error. It is probable that a large number of these supposed ulcers in women were in reality the result of pyloric spasm due to cholelithiasis or some intestinal lesion which gave rise to the gastric disturbance.

In 636 of the 1841 cases the ulcers were located in the stomach, and in 1205 they were located in the duodenum. It must be borne in mind that all the early cases were supposed to be gastric and were thus classified. The percentage in the last 1000 accurately observed cases showed 73.8 per cent. duodenal and 25.2 per cent. gastric. Of the gastric, 29 per cent. were females and 71 per cent. males. Of the duodenal, 21 per cent. were females and 79 per cent. males.

In differentiating between an ulcer in the pyloric end of the stomach and one in the first portion of the duodenum the situation of the pyloric veins is the determining factor. Just at the pylorus, from above and below, short, thick veins, usually 1 to 2 cm. in length, come into view from behind and pass forward. There is a distinct notch at the points of emergence of the veins. From these veins there usually extends an arching vein from each side, sometimes uniting, forming the pyloric vein, sometimes ending in a

spray. This superficial pyloric vein is not so characteristic as the thick veins I have just described, but, when present, it is a ready means of differentiation.

The terminal three-fourths inch of the pyloric end of the stomach is not often involved in ulcer. The more common seat of gastric ulcer is along the lesser curvature, often saddle-shaped. The ulcer is more often on the posterior than on the anterior wall. But whether situated anteriorly or posteriorly, a superficial ulcer at the point of contact often appears on the opposite wall—the "contact" ulcer. The gastric ulcer itself is, as a rule, clean cut, with a hard, grayish-white base, and is round or oval in shape. Outside of its crater there often is a massive infiltration into the outer layers of the muscularis and peritoneum. Over this, very frequently, protective adhesions are found, sometimes binding the seat of the ulcer to other organs, such as the pancreas or liver, a condition of incomplete or protected perforation. The induration is always very much more extensive than the actual crater, and is not entirely dependent on the size of the ulcer. The situation of the ulcer, however, may be at any point in the wall of the stomach.

Multiple ulcers are not frequently found at operation, which is contrary to the early views, based on clinical observations and postmortem findings in deaths due to acute ulcerative processes in the stomach. These processes were usually gastrotoxic in origin, and not often the source of chronic ulcer. Multiple ulcers of the stomach and duodenum or separate ulcers of the stomach and duodenum exist in the same case in about 5 per cent. of the cases.

The character of ulcers of the duodenum differs in many respects from that of ulcers of the stomach. They are usually to be found in the upper two inches of the duodenum and more often in the anterosuperior wall. When found on the posterior wall, they are usually of the same character as when found in the stomach. A typical crater and the contact ulcer on the anterior wall may give rise to an independent induration. As a rule, the duodenal ulcer has its origin below the pylorus, but when it extends

toward the stomach, it usually stops short at the pylorus, which it
may undermine.   In exploring for ulcers of this description I have
occasionally had difficulty in discovering the posterior ulcer, be-
cause it was concealed underneath the projecting pyloric ring.
The mucous membrane of the upper duodenum is thin and gran-
ular, and ulcers confined to the anterior wall, if they take upon
themselves the crater-like character of the gastric ulcer, will de-
velop a localized mass over the site of the ulcer.   Many times,
however, no crater is found in the mucous membrane in duodenal
ulcer, but rather a discolored, moth-eaten patch in the center of
which may be a dimple-like ulcer and outside of this a typical in-
duration.   It is probable that this variation from the ordinary
type of gastric ulcer explains why duodenal ulcers have been so
frequently overlooked at autopsy.

There is a variety of duodenal ulcer which sometimes occurs in
the region of the papilla of the common duct, giving rise to attacks
resembling gall-stone colic and profuse hemorrhages.   The three
cases I have had an opportunity to examine have all been seen
postmortem, the patients dying from acute hemorrhage after pro-
longed symptoms resembling cholelithiasis.

Incomplete protected perforation of duodenal ulcer, giving rise
to localized peritonitis covered by adhesions, is common.   The ob-
servation of such patients operated on during an attack has shown
a localized peritonitis in the vicinity .of the ulcer which makes it
probable that an actual leakage had taken place, but that the re-
sistance of the peritoneal cavity was sufficient to care for the com-
paratively small amount of more or less sterile secretion which es-
caped.   Occasionally this localized infection results in a phlegmon,
subdiaphragmatic or otherwise.

Indications for Operation.—In the early history of the disease
long periods of remission may occur in which it would appear from
the symptomless course that the ulcer had healed.   Yet case after
case operated on during the period of remission does not show the
ulcer to be healed, thereby repeating the history of appendicitis and
gall-stone disease inasmuch as the recovery from each attack is
erroneously supposed to be a cure.   Permanent healing of chronic

ulcers of the stomach and duodenum by non-operative means must be of rather infrequent occurrence. That a large number of acute, subacute, and some chronic ulcers are cured permanently cannot be doubted, but if they fail to show permanency after a reasonable attempt at cure under ordinary conditions of life, the patients should be treated surgically, not only from the standpoint of the disability of the patient, but also from the standpoint of mortality. The patient with ulcer treated medically is in far greater danger of death from hemorrhage, perforation, obstruction, or cancerous degeneration than he is from an operation. Those patients who can afford to carry on prolonged treatment are, of course, in better condition for non-operative therapy than is the working-man who must earn his living and live on those things which he can obtain.

THE SURGICAL TREATMENT

Gastric Ulcer.—Gastrojejunostomy is the most generally useful operation for gastric ulcer and has a wide field of application. Especially is this true when there is obstruction in the vicinity of the pylorus. It may be said that the greater the obstruction within limits, the more immediate and permanent the results of gastrojejunostomy. It is probable that gastrojejunostomy is of value not only as an operation for drainage, but that it also changes the physiology of the stomach and brings a greater measure of relief than can be achieved without it. While posterior gastrojejunostomy is the operation of choice, in certain cases adhesions may prevent its use. In these cases the anterior operation has given good results. For those ulcers which lie in the body of the stomach and in which the gastrojejunostomy must be made beyond the point of ulceration, the results are less favorable.

Because of the menace of cancer, all ulcers of the stomach, without regard to their situation, should be excised if possible. In our experience local excision of the ulcer without gastrojejunostomy has sometimes failed to effect a cure. I believe, therefore, that, as a rule, gastrojejunostomy should be done in addition to excision.

When a resection in continuity of the stomach with end-to-end union has been made for chronic ulcer, the results have been excellent without gastrojejunostomy.

For posterior ulcers of the body of the stomach which have become adherent, especially to the pancreas, transgastric excision of the ulcer has been of service.

In *hour-glass* stomachs gastrogastrostomy is a desirable operation, although resection in continuity when it can be done has given good results. In some cases, gastrojejunostomy fulfils the indications admirably.

When the ulcer occupies the pyloric end of the stomach, the pylorectomy of Rodman gives excellent results, both immediate and remote.

In those ulcers of the body of the stomach that cannot be excised, and in which gastrojejunostomy cannot be done, temporary jejunostomy is distinctly useful, especially in cases in which a differential diagnosis between malignant and simple ulcer cannot be established. The procedure gives prolonged rest to the stomach and maintains good nutrition. Jejunal feeding may be maintained for several months with distinct advantage.

Ulcer of the Duodenum.—Gastrojejunostomy is a most satisfactory operation in all those cases of ulcer of the duodenum in which there is actual or potential obstruction. We have followed Moynihan in infolding the ulcer with fine silk and placing one or two sutures in such manner as to block the pylorus to prevent food entering the ulcer area during the healing period. This blockage by suture cannot be expected to be permanent, but in connection with the permanent obstruction produced by healing of the ulcer it usually answers the purpose. If there be neither actual nor potential obstruction, this blockage should be accomplished by more efficient means. We have used the fascia closure of Wilms and the omental strip closure of Kolb, in each case applying the living tissue to the groove previously made by the suture-blockage. Several of these patients were reëxamined some time after the operation and the pylorus was found blocked.

At the present time we are excising a considerable percentage of

duodenal ulcers when they are situated so that it may readily be done. In our earlier cases simple excision was practised and a certain percentage of them failed to obtain complete relief. It was found necessary to make thorough provision for drainage at the pylorus after excision either by the Heineke-Mikulicz pyloroplasty or, what we have found still better, the gastroduodenostomy of Finney, which lends itself admirably to the excision of the duodenal ulcer.

Results of Operation.—Duodenal and gastric ulcers at the pyloric end of the stomach yield equally good results following operation. The greater the distance of the gastric ulcer from the pylorus, the greater the technical difficulties in its operative relief, the greater the mortality and, on account of the deformities which may be occasioned, the less certain the cure. But taking the patients as they come, at least 95 per cent. of those with gastric ulcer will be cured or greatly relieved by operation. The operative mortality in the gastric ulcers, counting all cases dying in the hospital without regard to length of time thereafter nor cause of death, was 3.8 per cent. This includes acute perforations, acute hemorrhages, and all types of operations, resections, etc. The results in duodenal ulcer are extraordinarily good, 98 per cent. of the patients either being cured or greatly relieved by the operation. The mortality of this group was only 1.5 per cent.

Recurrence of Ulcer.—In a small percentage of the cases of both gastric and duodenal ulcers there has been a definite recurrence of symptoms, and in which it would appear an actual redevelopment of the original ulcer had taken place. A small number of these patients have been reoperated on in our clinic, and in each instance the source of trouble proved to be a gastrojejunal ulcer in the suture-line of the original gastrojejunostomy, as a rule, due to the sloughing of the continuous sutures of silk or linen which had been used in the gastrojejunostomy. The symptoms were quite like those the patient was suffering from at the time of the primary operation, showing that the same disturbance may come from suture-ulceration as that manifested by the original lesion. We have, therefore, abandoned continuous silk sutures in gastrojejunostomy, now

using interrupted musculoperitoneal sutures of fine silk, with continuous chromic catgut for the inner rows.

Occasionally, fixation of the pyloric end of the stomach in the adhesions about an ulcer has continued to give rise to such pain and distress as to lead to the belief that the ulcer had recurred, or, at least, to the idea that the operation was a failure. In these cases the unilateral pyloric exclusion of von Eiselsberg as a secondary operation has given permanent relief.

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CAUSES OF FAILURE IN GASTRO-ENTEROS-TOMIES *

CHARLES H. MAYO

Gastro-enterostomy as employed for the relief of gastric and duodenal ulcer and obstruction to the delivery of gastric contents is an increasingly common operation.   The usual type of operation is the posterior short loop or no loop gastro-enterostomy.   The anterior gastro-enterostomy may occasionally be required, especially in advanced cancer of the stomach in which partial gastrectomy has been done and adhesions or some anatomic condition prevents the choice of the posterior operation.   Various forms of plastic gastroduodenostomy are gaining in favor, especially when the pyloric region of the stomach and duodenum can be mobilized and the tissues are not too softened by disease for safe suturing.   The methods employed in these cases are the Finney and modifications of the earlier types of operations advocated by Heineke and Mikulicz.

The surgical technic in gastro-enterostomy has been carefully worked out, and from a mechanical standpoint is now nearly perfect.   Moreover, the details of the various methods are readily mastered, and the operations may now be placed in the class of fixed surgical procedures with a low mortality, such as appendectomies and operations on the gall-bladder and ducts which present a very high percentage of success.   However, the percentage of failures, some of which are avoidable, is too high.   One such case which becomes an operative failure creates more confusion and condemnation of the procedure than many successful cases

can overcome. It is the group of cases that must be called failures which deters the internists and general practitioners from advising surgical treatment in many cases until the operation is one of necessity, with the 'attendant additional risk from the more advanced condition of the disease. The procedure is a rational one mechanically, and, as Patterson says, in addition does much in changing physiologic conditions of gastric digestion which accounts for part of the improvement. The gastric acids are greatly lowered, and the alkaline duodenal secretions which enter the stomach probably have a beneficial effect in the healing process, although the greatest relief is probably from overcoming delay and food retention. The next or second step of surgical progress has also been accomplished—that is, the reduction of the morbidity following operation. The third step, or permanency of cure, seems to have been accomplished in a high percentage of cases, as based upon earlier work. Eusterman has compiled the end-results in 1200 cases of duodenal and gastric ulcers operated on in our clinic two or more years before the compilation. He showed: (a) Of 600 duodenal ulcers, 90 per cent. were cured or greatly improved; (b) where a pyloric obstruction existed with duodenal ulcer, a cure or marked improvement followed in 95 per cent. of the cases; (c) 92 per cent. of the cases of gastric ulcer with obstruction were cured or improved; (d) 74 per cent. of gastric ulcers without obstruction were cured or improved, and (e) the immediate operative mortality of all cases was 0.5 per cent.

Gastric Ulcer.—It must be generally conceded that there are medical ulcers of the stomach which involve only the mucosa. These mucus ulcers, which give no symptoms when chronic, if they can be diagnosed, are believed to be medical. The surgeon does not see them. Such ulcers, or rather erosions, are much more common than is generally supposed. Their tendency is to heal. The ordinary ulcer, however, commonly involves the deeper tissues of the stomach or duodenum; in fact, it undoubtedly begins beneath the mucous membrane, causing its destruction. In the surgical cases there are thickening and changes in the surface peritoneum,

especially of the stomach, and both gastric and duodenal ulcers are subject to perforation. The scars of healed ulcers and their presence in an active state are as palpable and visible as those which form after ulcers on the leg. At the present time patients with gastric ulcers must be considered as border-line cases from the fact of being treated in the same stage by the gastro-enterologist and the surgeon. There is no doubt that ulcers may heal with and without the influence of treatment. Unfortunately, many of them are located in the pyloric region,—duodenal or gastric,—and the contraction incident to healing produces mechanical obstruction. Thus a progressively contracting ulcer of the lesser curvature may produce an hour-glass stomach, yet the ulcer itself always remains small—approximately the size of a penny.

Gastric ulcers, while more frequent on the anterior wall or involving the lesser curvature,—saddle ulcer,—which makes them palpable or fairly conspicuous to sight, are often located on the posterior wall, and it is necessary to break through the gastrohepatic omentum to palpate or see the posterior wall of the stomach. The majority of ulcers of the duodenum are anterior, yet here, too, the ulcer may be posterior. With marked symptoms of ulcer which have justified the operation a most careful search anteriorly and posteriorly must be made unless its presence is proved by gross changes in the bowel and pylorus which have been bound down to the pancreas by perforation. In such cases the obstruction may be of sufficient importance to indicate gastroenterostomy without absolute exposure of the ulcer area. It must be generally admitted that a gastric syndrome simulating true gastric or duodenal disease may be wholly of reflex origin from the gall-bladder, appendix, or other abdominal conditions. If an ulcer is not found on exploration (I should again emphasize that all ulcers are tangible which are surgically curable), and if there is no obstruction present, a gastro-enterostomy should not be made, but the surgeon should make a careful search for disease of the other abdominal organs, that is, of the pelvis, appendix, gallbladder, pancreas, and kidneys, to determine what factor may have caused the gastric syndrome. The surgeon constantly sees

such reflex cases that have been treated for ulcer over long periods. Even with the present diagnostic means, x-ray, both fluoroscopic and radiographic, test-meals, stool and laboratory examinations, it is impossible positively to diagnose some of these cases. In fact, the cause of some of them cannot be determined with the abdomen open. A gastric syndrome, however, may often indicate a surgical disease, when, for example, it is from a gall-bladder reflex, as if it were due to an ulcer itself. A careful examination of this phase of the subject shakes one's faith in the value of some large groups of medical statistics which have been backed by a very low percentage of operative proof. Practically, then, all except the acute or perforating ulcers, often without previous symptoms, receive medical treatment for a long time before operation is recommended. Medical treatment vigorously instituted may relieve ulcers—in fact, may heal them. Contributing and associated diseases and relapses may render the choice of surgical treatment imperative.

Should Ulcers of the Stomach be Excised?—As a rule, ulcers of the stomach, when favorably located, should be excised. Excision should be made when the ulcer is located so that the additional procedure does not add much risk to the gastro-enterostomy. The lowered acidity of the stomach and its relief from stasis tend to heal ulcers after gastro-enterostomy. There is probably only a low percentage of risk of cancer developing in ulcer after gastro-enterostomy. The excision then should not be allowed to contribute much to the risk. It is possible, however, that grossly indurated ulcers may already be carcinoma.

Balfour's method of destroying the ulcer by slowly perforating the ulcer area with a Paquelin cautery and closing the opening by suture, as after excision, is quite as effectual as excision and safer, especially for the treatment of small and moderate sized ulcers.

In gastric ulcers located at a distance from the pylorus, the pyloric region being freely movable, some form of plastic gastro-duodenostomy is nearly as effectual as a gastro-enterostomy in draining the stomach. With this region freely movable, small

ulcers, gastric or duodenal, may be excised as a part of the line of incision for the plastic operation. Experience with gastro-enterostomies and plastic pyloric operations has shown that, after the latter, patients do not as immediately convalesce. The mortality is unquestionably higher, especially when associated with the excision of ulcer.

Location of the Opening for Gastro-enterostomy.—Hartmann has shown that the further the opening is made into the greater curvature of the stomach, the less effectual is the drainage, since the gastric contents pass over the opening into the pyloric end of the stomach and are forced on by active peristalsis toward the duodenum. A gastro-enterostomy thus located requires efforts at pyloric closure to improve delivery. But if the opening is made toward the pylorus, the peristaltic contractions may start the contents toward the duodenum and into the intestine through the new opening. Other things being equal, such a gastro-enterostomy will deliver the gastric contents even if the pylorus is open.

Length of the Loop in the Posterior Operation.—The short loop is best, the clamp on the jejunum being set as closely as possible to its origin, leaving room for pieces of protecting gauze beneath the clamp. As nearly as possible at the close of the operation the loop of jejunum should be left as it was found upon lifting the transverse colon. This will usually be seen passing to the left as the first splenic loop of small intestine. Occasionally it may run downward or turn to the right, and if so, an adhesion or an unusually long peritoneal band will extend down on the jejunum from the mesentery of the transverse colon, which swings it around. This is not the ligament of Treitz, but a peritoneal band, and must be divided if one desires a short loop. The attachment of the mesentery of the transverse colon is wedge shaped over the spine. On the left side of the wedge, and on the left side of the spine, is the termination of the duodenum and the beginning of the jejunum.

One of the great immediate bugbears of posterior gastro-enterostomy has been the vicious circle. In our earlier work, by turning the bowel to the right at the point of attachment, there

was an average of one case of vicious circle in about 14 operations. In order successfully to turn the bowel to the right we were compelled to leave a longer loop and often to make a primary or even a secondary entero-enterostomy of the loop. This twist of the bowel was a relic of the old anterior operation, and to obviate it the Y method of Roux was developed, and also by using a fairly long loop. This method is in common use and is employed by many surgeons to overcome the difficulties resulting from twisting the bowel out of its normal position. If this loop is not too short, the vertical gastro-enterostomy incision permits of a good working outlet depending upon personal technic. It must be rightly placed to the bottom of the stomach and should be to the right of a line drawn down the lesser curvature crossing the pyloric end of the stomach. This is not so important if the case is one of obstruction.

The gradual closure of the gastro-enterostomy, although a rare occurrence, is an additional cause of failure in the operation.

Jejunal ulcers following gastro-enterostomy have been rather frequently reported. I have not observed any such except in connection with gastro-enterostomy itself just below the opening. In most of the cases that were explored the buried or partially buried remains of the non-absorbable suture material used in making the anastomosis was found. The true importance of this was not appreciated until it was seen in a series of cases. The symptoms in these cases very much resembled the original symptoms of ulcer which the patient complained of before operation. The x-ray might show that the gastric contents passed, by either or both routes, the pylorus or the new opening. At the second operation the gastro-enterostomy incision seemed to be indurated and much thickened throughout a part of its circle; yet the wall of the stomach could be invaginated through the opening. Inasmuch as the opening was patent, many surgeons, including those of our clinic, have contented themselves with an entero-enterostomy of the jejunal loop, which has usually given only partial relief, since the real cause of the ulcer is often the remains of the suture which acts as a septic drain into the thickened tissue. In

these cases cure may be obtained by opening the loop of bowel at the site of the gastro-enterostomy, making a Finney type of plastic operation, as recommended for pyloroplasty, and removal of the thread if found.   The ulcer with its base are excised and closed with sutures.   Eventually a spontaneous cure may follow the disappearance of the suture in some cases.   In a number of cases of our own and from other clinics we have found strong silk sutures many months after gastro-enterostomy—in one case three years and six months, in three years and one month, in another two years and three months after the gastro-enterostomy, and others from seven months on.

Jejunal ulcers may be primary from bad infarcts or may be mechanically produced from the retention of permanent suture material in making the anastomosis.   Patients who have been primarily relieved by gastro-enterostomy and have developed the same symptoms later should be reoperated on, and this condition, among other causes of relapse, be looked for.   What is the prevention of this condition?   The use of chromic catgut as an absorbable suture, two rows protected by interrupted silk or one row with interrupted silk sutures for the second row.   A change of method is imminent and necessary.

Gastro-enterostomy for a prolapsed stomach as such without obstruction is not indicated.

THE RADICAL OPERATION FOR CANCER OF THE PYLORIC END OF THE STOMACH *

WILLIAM J. MAYO

Pylorectomy and partial gastrectomy have been accepted operations for more than a quarter of a century. Péan[1] in 1879 made the first pylorectomy; the operation was next performed by Rydygier,[2] whose original contribution was both attractive and sound. To the master surgeon, Billroth,[3] who did the first successful operation in 1881, must be given the credit for not only developing the technic, but for a thorough elucidation of the principles which guide us in its performance.

Cunéo,[4] by a brilliant study of the lymphatics of the stomach, added greatly to our knowledge of the spread of malignant disease of this organ; and, based on his work, Mikulicz and Hartmann were able to point out the necessity for the extirpation of the glands on the lesser and greater curvatures respectively. In spite of the great importance of the contributions of these and other men; in spite of the fact that the operation has been one of diminishing mortality and that undoubted cures are to be found in literature, the operation has not been popular.

Cancer of the stomach is the most frequent form of cancer in the human body. In at least 75 per cent. of gastric cancers the pyloric half of the stomach, which is the readily removable portion, is involved. The opportunities, therefore, for the operative treatment of gastric cancer are many, but the surgeons performing the operation are few and the results meager.

Perhaps the most important reason for this apathetic attitude

of the profession in regard to cancer of the stomach has been our inability to make a diagnosis sufficiently early for the performance of a radical operation with a reasonable operative mortality and a fair prospect of cure. At present, however, largely through radiography, the clinical diagnosis of cancer of the stomach can be made early in a large percentage of cases. Exploratory incisions, which up to within the past year were our chief reliance, though carrying with them the patient's dread of an unnecessary operation, are fortunately no longer required in anything like the percentage of cases in which they were formerly necessary. The history of the patient, the radiographic and physical findings, and the use of the stomach-tube to-day give a reasonable prospect of a correct early diagnosis.

The laboratory tests, so long depended on and which had proved so fallacious a guide, have been justly relegated to a minor position. These tests should not be abandoned, however. They are of value in differentiation, and since they may now be checked up by other means, this value should increase as we learn correctly to interpret their results.

Another reason for the reluctance with which the radical operation for cancer of the stomach has been adopted by the profession is the immediate mortality. These patients are usually poor risks; the operation is one which requires a high grade of skill and technical knowledge, and the margin between recovery and death is at best a narrow one. The patient who does not do well usually dies because the conditions which interfere with his recovery are in themselves most serious and the resistant powers low.

Little comment is necessary concerning the main features of the operation of partial gastrectomy. They are well known and are not in controversy. The lymphatic glands lying in four groups with the four blood-vessels are quite easily extirpated. The high ligation of the four vessels renders the field of operation dry and bloodless—an important consideration, since loss of blood in debilitated patients is the most potent cause of surgical shock. The operation can be done in the average case within an hour.

There have recently appeared an encouraging number of contributions to this subject, especially relating to the technic and containing suggestions for shortening the length of time of the operation, which has been at least one of the factors in the death-rate. Of these contributions, Crile's[5] and Lilienthal's,[6] advocating the two-stage operation, have been among the more important. They have rightly called attention to the fact that in debilitated patients gastro-enterostomy, which can be done quickly, improves the patient's nutrition and general condition; and a resection can be made at a later time without so serious a risk.

In our clinic we have in the last fifteen years made a number of the two-stage operations for cancer of the stomach, and of these not one patient died as a result of the resection. Standing alone, this would seem to be a strong if not an absolute indication for the two-stage operation. But an examination of the facts concerning these cases leaves the indications less clear, since they were in a sense selected from a number of patients on whom we could have done a primary resection and who were subjected to a gastro-enterostomy with the intention of following this procedure by a resection, but who for one reason or another never came to the radical operation. First, some of those who were in a most serious condition died following the gastro-enterostomy. They would, of course, have died if a primary resection had been made instead of a gastro-enterostomy, but the resection received the benefit so far as mortality statistics are concerned. Second, some of the patients, especially those with large ulcerating cancerous masses, did not sufficiently improve after gastro-enterostomy to enable them to submit to a second operation, again bettering the statistics of resection by the elimination. Third, an occasional patient would improve so greatly following gastro-enterostomy that a radical operation would be refused until too late. Fig. 42 shows a specimen from a considerable group of patients on whom we have done a primary partial gastrectomy, but who, for reasons already stated, would probably not have come to a secondary radical operation if a gastro-enterostomy had been done primarily instead of the resection.

Another fact of great importance was the occasional delay before the second operation, as a result of various causes following the gastro-enterostomy—a delay which resulted in the vasculariza-

Fig. 42.—Gross specimen.   Three-fifths of stomach removed for large fungating carcinoma.

tion of the adhesions which so often formed following the first operation, and which in this process became infected with carcinomatous cells.   The question of the implantation of cancerous cells during operation is a most important one.   I have related

elsewhere[7] some cases in our early experience where cells were loosened up from gastric carcinoma and implanted upon the margins of the portion of stomach which remain following resection. For this reason we have since cauterized the cut end of the stomach and duodenum with the actual cautery, to lessen this liability. In several of our cases the abdominal wound was so infected. Grafting in carcinoma of the stomach is exceedingly common—especially grafting to the peritoneum; and the necessary handling of the growth, irritation of the peritoneum, and the injury inflicted by the performance of the gastro-enterostomy itself are all matters of importance in this connection.

I am under the impression—after, it is true, a somewhat superficial examination of the subject—that the percentage of five-year cures in the two-stage group has not been as high in our experience as in the one-stage operation. It would seem that the two-stage operation is one which should not be generally adopted, but rather one for the occasional case in which the general condition of the patient rather than the local condition of the tumor is the indication for this particular method. Under such circumstances we employ the two-stage operation and believe that an occasional case is carried to a successful termination who might have been lost following the one-stage operation.

If the two-stage operation is decided upon, it is necessary to plan the gastro-enterostomy opening so that it will be in a situation which will not cramp or hamper the resection.

The mortality depends more upon the cases which will be accepted for operation than upon any other one factor. We have had mortalities in some years following partial gastrectomies as low as 6 per cent.; in other years, with an increasing experience and improved technic, a mortality of twice that or even more, due to the class of cases which we accepted for operation and which would previously have been subjected, if operated on at all, to a palliative gastro-enterostomy.

Should patients with advanced cancer of the stomach be subjected to radical operation? In view of the fact that some of these patients, especially those with large fungating growths, have lived

beyond the five-year limit, we are compelled to answer the question in the affirmative. We should further consider the fact that patients subjected to the removal of the visible growth in the stomach, even if all the glands cannot be removed, will get a year or more on the average of a very comfortable existence, and that this comfortable existence is cheered by the knowledge that there
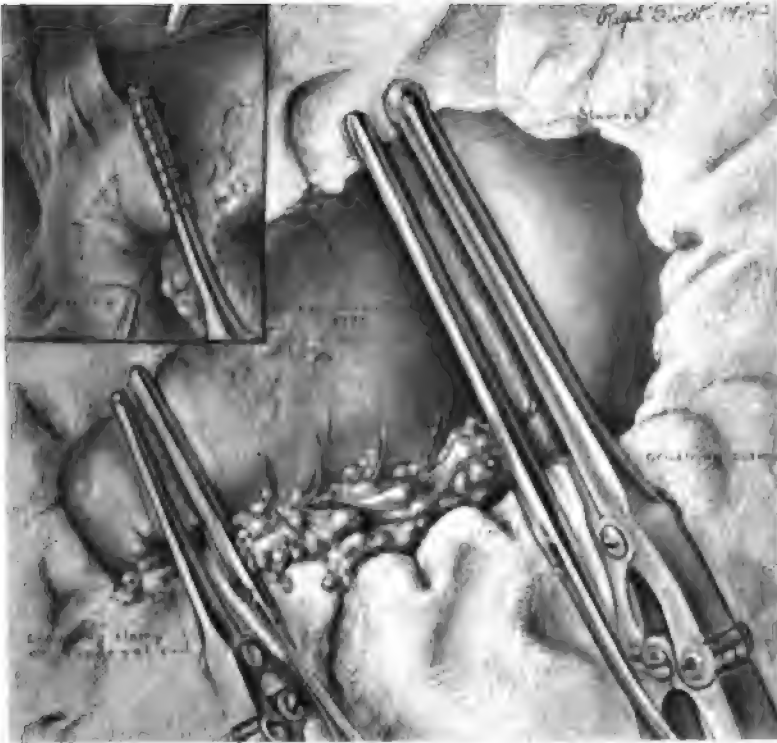
Fig. 43.—Blood-vessels tied, glands separated, crushing clamps in place, and also clamps to prevent leakage from part to be removed. Upper left drawing shows stump of duodenum in crushing clamp with suture placed for closing.

is a possibility of cure, since, in some cases, irremovable glandular hyperplasia is the result of infection rather than metastasis. These experiences, acknowledged to be accompanied by a high mortality, have led us to extend the radical operation to a group of cases which we would have formerly considered inoperable.

The most serious technical question concerns the form of re-union of the gastric stump to the intestine after the removal of extensively diseased portion. The gastric stump is small; it has already been seriously devitalized, and the gastro-enterostomy still further devitalizes the already damaged gastric wall. I am referring

Fig. 44.—Crushing clamp on the stomach. Cautery used to sterilize and prevent carcinomatous implantation. Stump of duodenum closed. Sutures placed to turn the duodenal stump into the denuded head of the pancreas.

now to the Billroth method No. 2; that is, complete closure of the duodenal and gastric stumps with an independent gastrojejunostomy, which has become, up to the present time, by virtue of its many advantages, the operation of choice by the majority of surgeons of the world.

The Billroth operation by method No. 1, that is, implantation of the duodenal stump into the narrowed end of the stomach, is not applicable in these cases, since the gap is too wide and the tension would be too great.
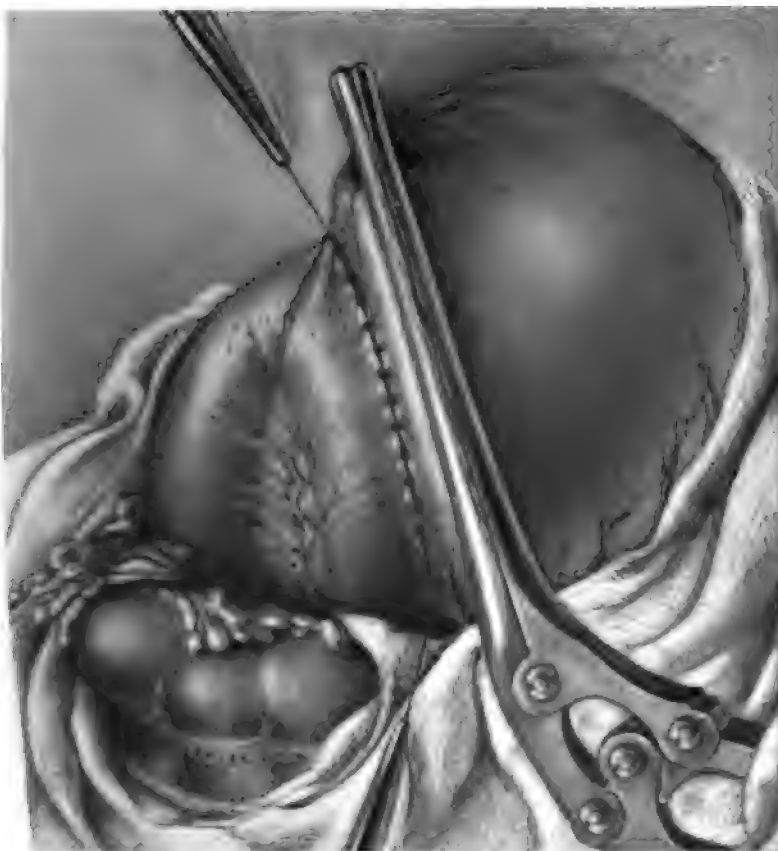
Fig. 45.—Upper jejunum, six to twelve inches from origin, brought through an opening which has been made in the transverse mesocolon and united by outer row of seromuscular silk sutures to the posterior wall of the stomach.

The operation of Kocher, in which the end of the duodenum is implanted in the posterior wall of the stomach, for the same reasons is inapplicable, although its distinguished originator

advanced the field for his particular method by suitable mobiliza-
tion of the duodenum.

It was with much interest, therefore, that I investigated the
method of Pólya,[8] in which, after the excision is made, the end
of the stomach is directly applied to the side of the jejunum, about
six to twelve inches from its origin.   Pólya reported six operations
with three deaths, but it will be noted from the case histories that
the disease was very far advanced in the patients who died.   A
number of operations (12) have been done recently in our clinic by
this method, with one death from pulmonary embolus, the autopsy
showing perfect condition of the operative field.   The technic em-
ployed is as follows:

The diseased portion of the stomach is removed in the usual
way, and the stump of the duodenum closed and buried (Figs. 43
and 44).   An opening is made in the avascular arcade of the
transverse mesocolon, and the upper jejunum pulled through until
it can be easily brought into contact with the stomach.   The end
of the stomach, which is held in the crushing clamp of Payr,
is united by suture to the loop of jejunum (Fig. 45) quite as
the ordinary gastro-enterostomy is made.   If the diameter of the
end of the stomach be very large, it can easily be diminished by
placing the sutures in such manner as to take a proportionately
greater bite in the stomach than in the intestine, thus reducing the
lumen of the stomach as the suturing progresses.   The stomach is
anastomosed to the jejunum at a point where the jejunal blood-
supply is extraordinarily good, and the jejunum can be depended
upon to do more than its share in the healing process.   Before
the inner through-and-through sutures are placed, the stomach
and intestine are grasped with elastic holding clamps to prevent
soiling;   the inner row of sutures is then run entirely around
and the outer row completed (Figs. 46 and 47).   The entire
anastomosed end of the stomach is then drawn down below the
transverse mesocolon, and the margins of the opening in the trans-
verse mesocolon carefully attached by a number of sutures to the
wall of the stomach (Fig. 48).   Fine silk is used for the peritoneo-

muscular sutures and chromic catgut for the through-and-through inner row.

This operation has some obvious advantages. It saves the
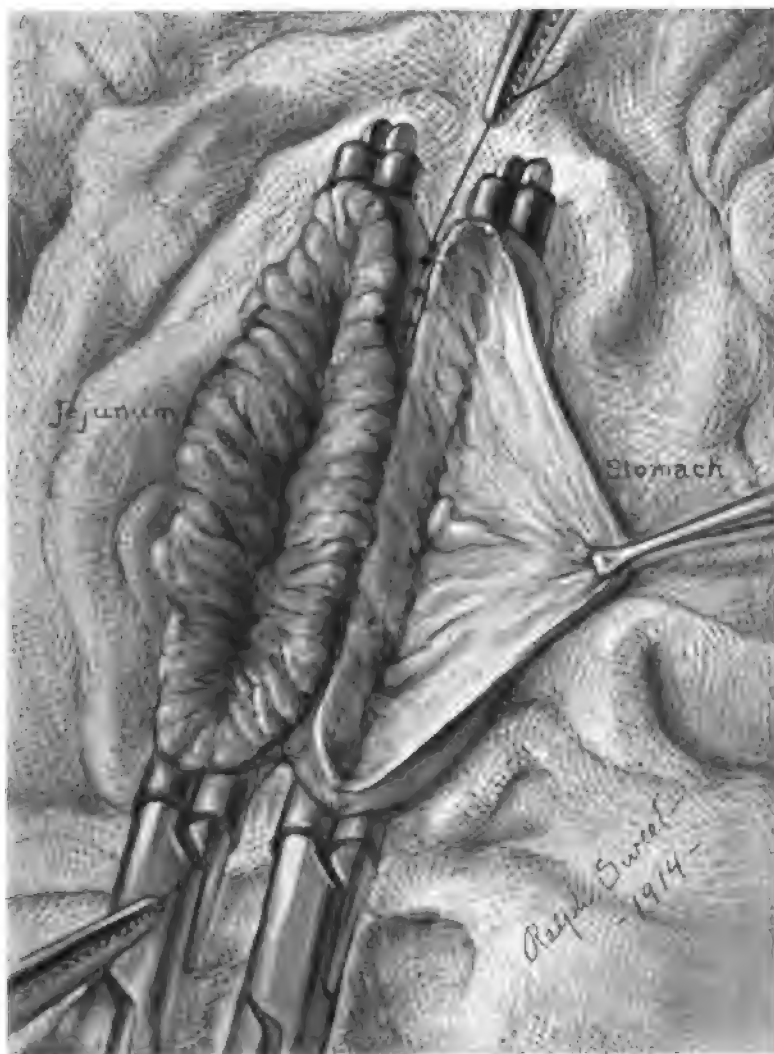
Fig. 46.—Crushing clamp removed from the stomach and holding clamps applied to jejunum and stomach to prevent soiling.

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Fig. 47.—Inner row of catgut through-and-through sutures applied to the posterior walls, uniting
jejunum to cut end of the stomach and continuing part way down the anterior wall.

time consumed in closing the end of the stomach, and in cases in which only a small pouch of the stomach is left, is very much easier than an independent gastro-enterostomy. Unless further
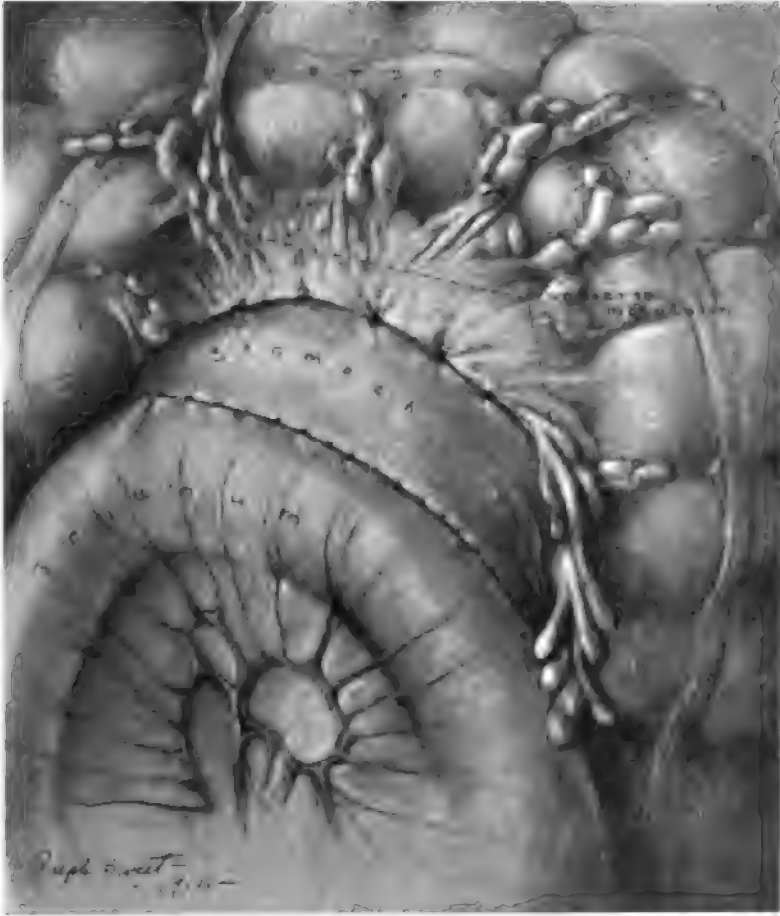
Fig. 48.—Anastomosis completed by an anterior row of seromuscular silk sutures. Anastomosed end brought through the opening in the transverse mesocolon and margins of opening sutured to the stomach.

experience shows some contraindications, I predict for this procedure a large field of usefulness if it does not become the method of choice.

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STUDIES IN THE PATHOLOGY OF GASTRIC ULCER AND GASTRIC CARCINOMA*

III. A Further Report of the Pathologic Evidence of the Relationship of Gastric Ulcer and Gastric Carcinoma †

LOUIS B. WILSON AND IVAN W. McDOWELL

INTRODUCTION

The following report is a continuation of a study of gastric ulcers and cancers first presented to this society in 1909.‡

Between January 1, 1905, and January 1, 1914, tissues were received for examination in the laboratories of the Mayo Clinic from 870 gastric and duodenal cases.§ From 705 of these cases the tissue included the site of the primary lesion. Of these, 260 were simple chronic ulcers without histologic evidence of cancer. Most of these ulcers have recently been critically examined by MacCarty.‖ Therefore the gross material and sections from only a small number of the ulcers have been examined by us for comparison with those from the cancer cases. The present review has been largely confined to the study of the gross and microscopic tissues from the 445 gastric carcinomas received in the laboratory during the nine years above mentioned. Of these, 399 specimens were resected by the

surgeon and 46 were removed at autopsy from cases on most of whom an exploratory or palliative operation had been done.

DATA

The data for the following report is based on—(a) The primary pathologic diagnoses made from the examination of the specimen immediately after its removal, in almost all instances, either by one of us (Wilson) or by MacCarty. This examination included in every case of at all doubtful character a microscopic examination of frozen sections. (b) The review of all photographs of the entire specimens and of microscopic sections taken at the time of the primary pathologic diagnosis. (c) The review of all sections of fixed tissues previously prepared from the cases. (d) From many cases the study of serial paraffin sections recently prepared and selected to include, wherever possible, a section through the border and base of the ulcerating lesion. (e) A study of the clinical data as regards length of period of previous symptoms and as regards subsequent history. This datum has been kindly supplied by Drs. Graham and Eusterman.

CLASSIFICATION OF CASES

All cases in which there was suggestive or positive evidence of cancer have been placed in four groups as follows:

1 (?). Ulcer with cancer questionable.

1. Ulcer with beginning cancer.

2. Ulcer with advanced cancer.

3. Cancer throughout the lesion.

GROUP 1 (?).—Group 1 (?) consists of those cases in which a most painstaking study of the sections gave evidence which was only suggestive of early cancer. The interpretation of the histologic pictures would, no doubt, vary with different observers. In general, it may be said that the suspicion of cancer rests upon profuse aberrant proliferation of the gastric epithelium and, in some instances, on suggestions of infiltration of individual cells or groups of cells into the surrounding tissue. Where infiltration can be accurately determined, there should be no question about the presence of cancer. Where it is doubtful, we must express that doubt. Among the cases in this group is the following:

CASE 1.—(86829.) S. H. F., female, aged forty-one years. History of chronic gastric ulcer seven years; more severe for last six months. Wide excision of supposed gastric ulcer July 7, 1913. Pathologic diagnosis, gastric ulcer. In fair condition six and one-half months after operation. (See Figs. 49–51.)

The significance of such cases from the clinical standpoint lies in the fact that of the 19 in our series, 3 patients have subsequently died of gastric cancer. In all of these, practically all

Fig. 49.—Case 1. Five-diameter magnification of section from border of ulcer.

of the small gastric ulcer was examined microscopically and no evidence beyond such as that seen in the above case was found.

The first of these patients, Case 2 (5957 P.), P. J. M., was a male, aged fifty-eight years, who for six years had had symptoms of chronic gastric ulcer. On December 3, 1906, a portion of the stomach was removed for a supposed gastric ulcer. Pathologic diagnosis was doubtful cancer on ulcer. Patient lived three years and one month after operation, dying of recurring gastric carcinoma.

The second patient, Case 3 (A10131), S. J., was a male, aged sixty-three years, giving a history of chronic gastric ulcer covering a period of two years. May 30, 1908, a partial gastrectomy with excision of a perforating gastric ulcer was done. Patient died of recurring gastric carcinoma twelve months later.

The third patient, Case 4 (15038), T. G., was a male, aged fifty-nine years, who had had symptoms of chronic gastric ulcer

Fig. 50.—Case 1. Fifty-diameter magnification of area marked *B* in Fig. 49.

ten years. September 24, 1908, there was a partial resection of the lesser curvature of the stomach for chronic gastric ulcer. Primary pathologic diagnosis of the tissue removed was ulcer. Patient returned two and one-half years later with an inoperable carcinoma of the stomach, from which he died two years and nine months after his first operation.

GROUP 1.—In Group 1 are placed those cases in which the epi-

thelium is not only aberrantly proliferating, but also undoubtedly infiltrating the surrounding tissues, and yet in which, on the other hand, the base of the ulcer is free of carcinomatous tissue and gives no evidence of ever having contained such. The following cases will serve to illustrate this group:

CASE 5.—(28092.) W. F. S., male, aged fifty-seven years. History of chronic gastric ulcer for three years; carcinoma, one
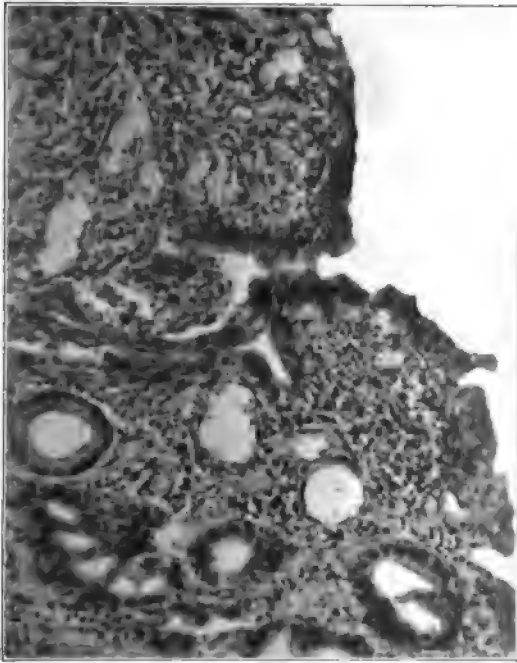
Fig. 51.—Case 1. One-hundred-and fifty-diameter magnification of area selected from Fig. 50, showing markedly proliferating epithelium with doubtful infiltration.

and one-half months. Resection three-fifths of stomach June 3, 1910. Pathologic diagnosis, early cancer on ulcer, glands not involved. Dead in thirty-six months after operation of recurring gastric carcinoma. (See Figs. 52–54.)

CASE 6.—(53784.) H. M. S., male, aged forty-five years. History of chronic gastric ulcer for nineteen years. Gastric car-

Fig. 52.—Case 5. Five-diameter magnification of section from border of ulcer.

Fig. 53.—Case 5. Fifty-diameter magnification of area marked *B* in Fig. 52.
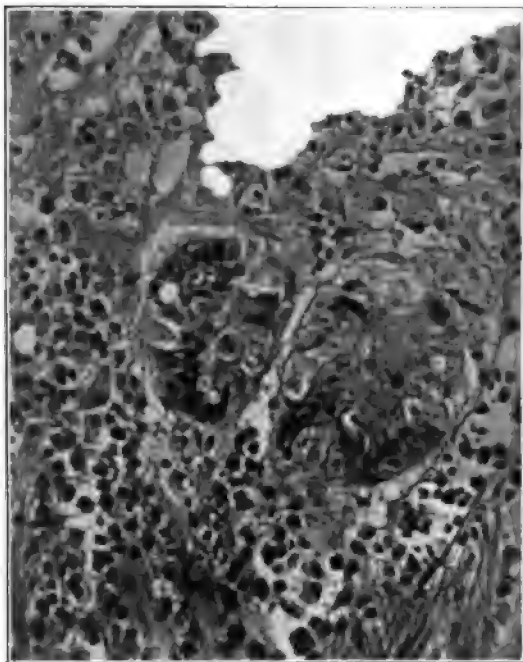
Fig. 54.—Case 5. Three-hundred-diameter magnification of border area shown in Fig. 53. Note the two groups of cells, the cancerous nature of which is typical though their infiltration is not plain.

Fig. 55.—Case 6. Six-diameter magnification of section across ulcer.

cinoma for three months.   Resection of two-thirds of stomach June
8, 1911.   Primary pathologic diagnosis, early cancer on ulcer,
no involvement of glands resected.   Patient reported in good
condition twenty months after operation.   (See Figs. 55–57.)

GROUP 2.—The cases included in this group are the cases in
which the cancer has more or less invaded the base of the ulcer,
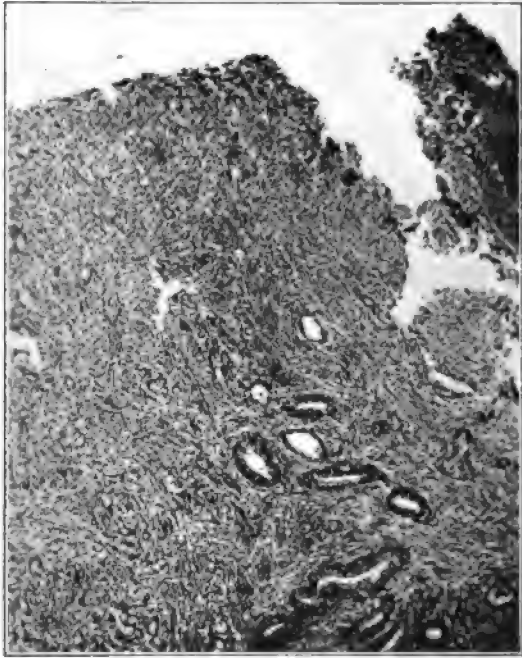
Fig. 56.—Case 6.   Fifty-diameter magnification of point marked *B* in Fig. 55.

and yet in which a well-defined portion of the ulcer remains free
of cancer.   It is concerning the cases in this group about which
most discussion has developed among pathologists, certain ob-
servers holding that it is impossible to distinguish in these cases
between the development of cancer in the base of an ulcer and the
erosion of cancerous tissue forming an ulcer which contains no
evidence of epithelium.   It seems to us, however, that it is possible
in many instances to differentiate between the two conditions,

and we have placed in this group only those cases about which we have felt certain that the condition was the former.   When a sharp border-line exists between the infiltrating epithelium and the scar tissue, and when, at the same time, the cancer tissue lies in an anatomic plane external to the scar tissue, it would appear that the evidence is preponderatingly in favor of the supposition
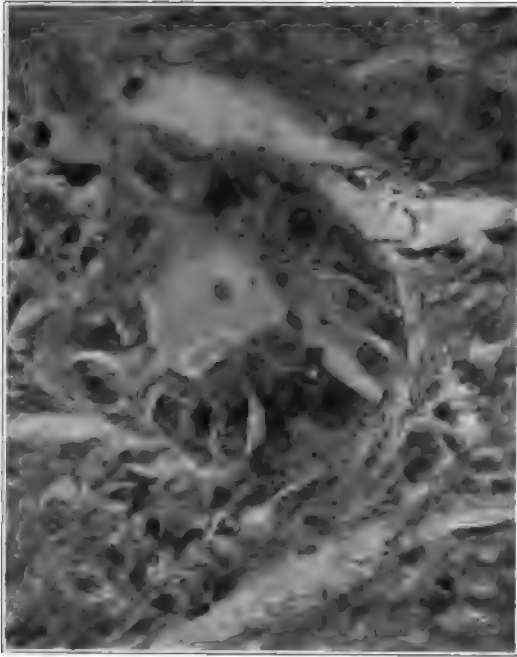
Fig. 57.—Case 6.   Six-hundred-diameter magnification of group of cells showing early carcinoma selected from area shown in Fig. 56.

that the scar tissue existed before the development of the cancer and consists of the remains of the base of a preëxisting gastric ulcer.   The following cases will serve to illustrate this group:

CASE 7.—(59396.)   J. D. H., male, aged sixty-five years.   History of chronic gastric ulcer for twenty-five years; of gastric carcinoma eleven months.   Resection of portion of stomach October 3, 1911.   Pathologic diagnosis, cancer on ulcer; three glands on

lesser curvature involved.   Patient died one month after operation.
(See Figs. 58–60.)

CASE 8.—(33130.)   E. W., male, aged thirty-nine years.   History of chronic gastric ulcer for many years; of gastric carcinoma
one year.   Partial gastrectomy January 26, 1910.   Pathologic
diagnosis, carcinoma on ulcer; one gland in greater curvature
involved.   (See Figs. 61–63.)
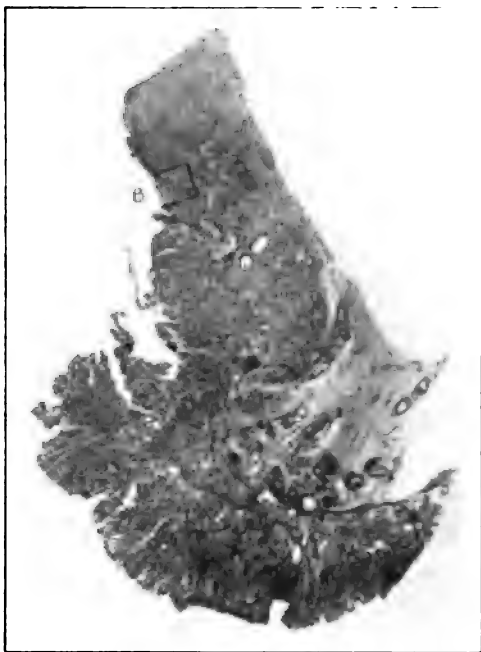
Fig. 58.—Case 7.   Five-diameter magnification of section through border to base of ulcerated portion.

CASE 9.—(29584.)   W. C., female, aged forty-nine years.   History of chronic gastric ulcer for many years; gastric carcinoma
two and a half months.   One-half of stomach resected October 8,
1909.   Pathologic diagnosis, cancer on ulcer.   Patient died of
gastric carcinoma six months after operation.   Case shown to
illustrate that even in advanced gastric carcinoma there may be
sometimes found areas in base of ulcer which are free of carcinoma
and give no evidence of ever having been invaded.   (See Figs.
64–66.)

Fig. 59.—Case 7.   Fifty-diameter magnification of area marked *B* in Fig. 58, showing sharp borderline which exists between ulcer and carcinoma in an advanced case.
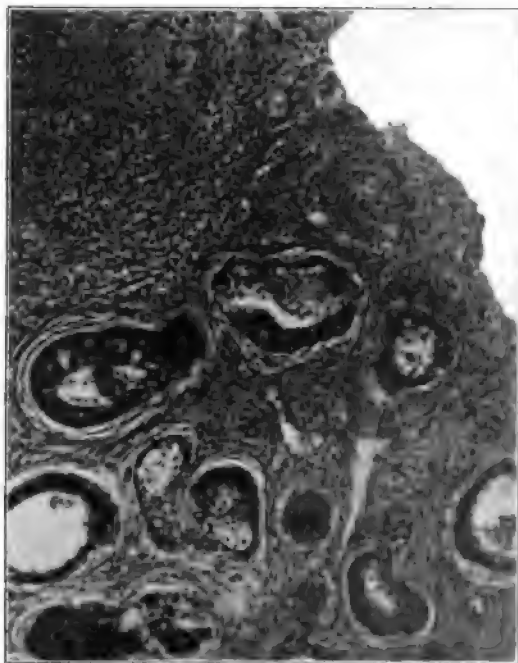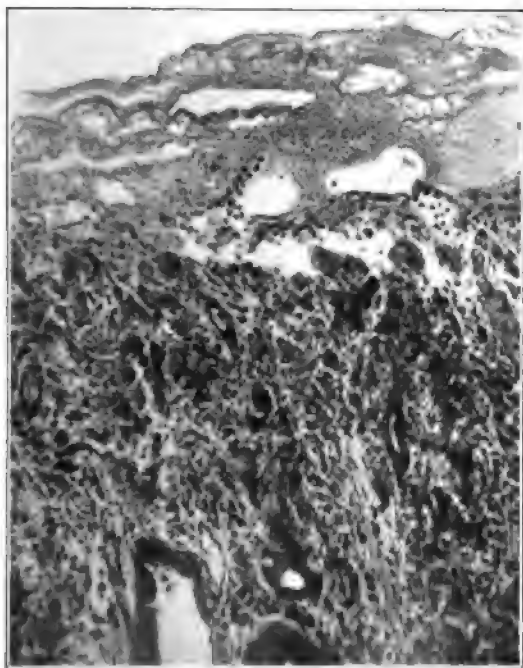

Fig. 60.—Case 7.   One-hundred-and-fifty-diameter magnification of carcinomatous area in Fig. 59.

Fig. 61.—Case 8. Two-diameter magnification of section through base of ulcer.
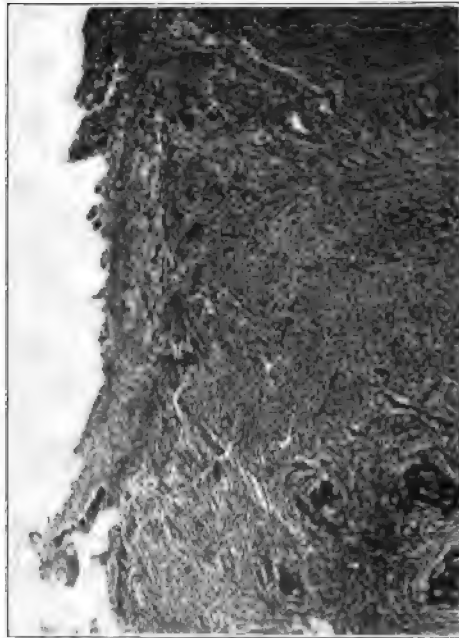
Fig. 62.—Case 8. Fifty-diameter magnification of area marked *B* in Fig. 61, showing sharp borderline between ulcer and carcinoma.

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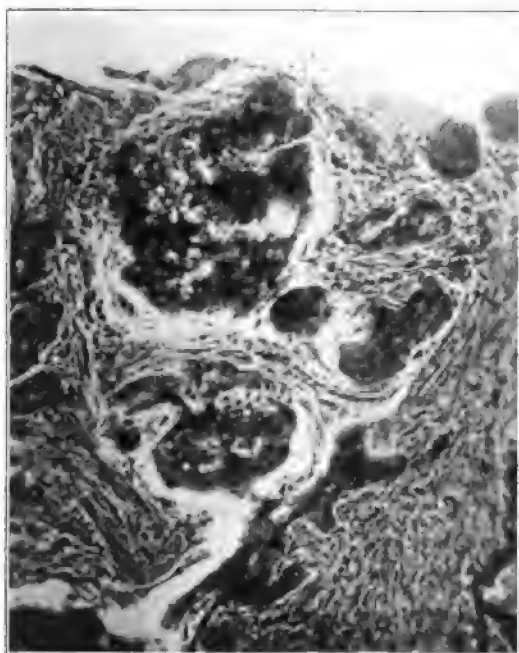
Fig. 63.—Case 8.   One-hundred-and-fifty-diameter magnification of carcinomatous border of section shown in Fig. 62.

Fig. 64.—Case 9.   Two-diameter magnification of section through base of ulcer.   Almost the whole of this section, except the area marked *B*, is infiltrated with carcinoma.
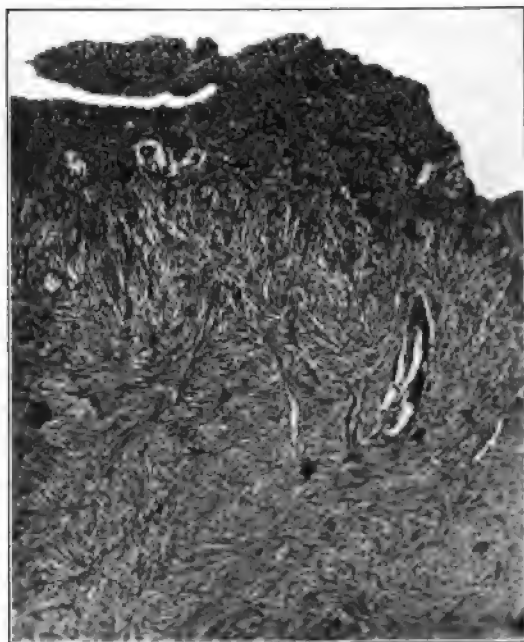
Fig. 65.—Case 9. Fifty-diameter magnification of area free from cancer shown at *B* in Fig. 64.
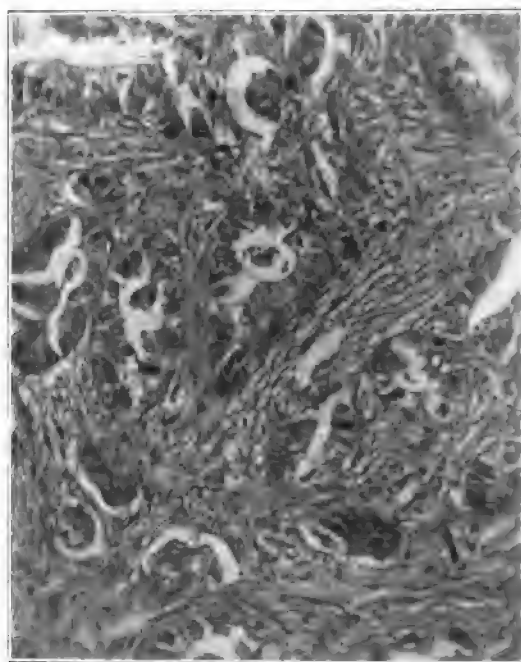
Fig. 66.—Case 9. One-hundred-diameter magnification of area just lateral to that shown in Fig. 65.

These scar-tissue bands extend through to the muscularis. When one studies the structure of the gross specimen in relation to the microscopic section, the impression is very strong that these cancer-free scar-tissue areas are not the result of the destruction of the epithelium, as we know does occur in scirrhus cancer elsewhere, but that these masses of scar-tissue have been formed prior

Fig. 67.—Case 10.   Four-diameter magnification of section through border and base of ulcer.

to the development of the infiltrating epithelium in their neighborhood.

CASE 10.—(69652.)   G. E., male, aged forty years.   History of chronic gastric ulcer for ten years; gastric carcinoma one month. One-third of pyloric extremity of stomach resected July 1, 1912. Pathologic diagnosis, carcinoma on ulcer.   Patient in good condition seven months after operation.   (See Figs. 67–69.)

GROUP 3.—This group contains those cases of cancer in which

the evidence of previous ulceration is absent or incomplete.   In a very few instances—less than 5 per cent.—is the evidence entirely absent.   In almost every case in the series there is ulceration, in some portion of which may be found a tract of scar tissue clear of carcinoma, in many instances penetrating through the muscularis and side by side with areas of cancer which lie in anatomic planes

Fig. 68.—Case 10.   Fifty-diameter magnification of area marked *B* in Fig. 67, showing line of demarcation between carcinoma and ulcer in base.

internal to the scar tissue.   Such a condition is seen in the following case:

CASE 11.—(27585.)   Male, aged sixty-three years.   History of chronic gastric ulcer extending over many years.   History of cancer extending over a period of three months.   Resection of pyloric two-thirds of stomach September 18, 1909.   Pathologic diagnosis, carcinoma with extensive glandular involvement. Patient died three months after operation.   (See Figs. 70–72.)

Fig. 69.—Case 10. One-hundred-and-fifty-diameter magnification of carcinomatous area as shown in Fig. 68.
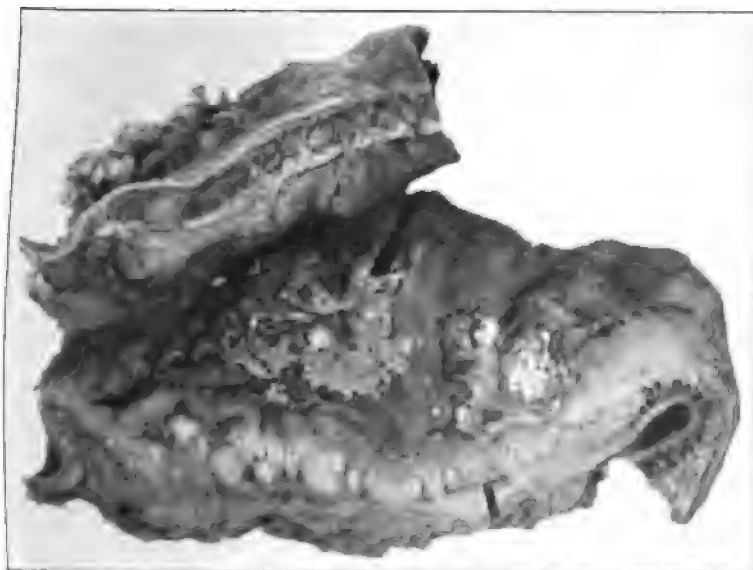
Fig. 70.—Case 11   Two-third-diameter magnification of gross specimen, showing extensive involvement of gastric wall.
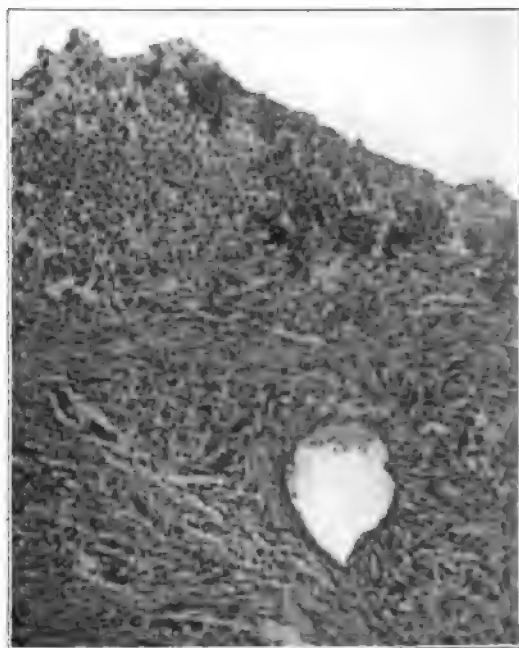
Fig. 71.—Case 11.   Fifty-diameter magnification of area in base of ulcerated portion of stomach. Shows that although the cancer tissue is much scattered it does not extend through to the muscularis and that some portions of the base of the ulcer consist of scar tissue which is cancer-free.

Fig. 72.—Case 11.   One-hundred-and-fifty-diameter magnification of cancerous portion of tissue.

Such a case as this has always been interpreted as ulcerating cancer. However, from the preponderance of cases in which the reverse has been true of the order of development, it would appear questionable whether we have the right to assume that cases of this kind are illustrations of ulcerated cancer. Indeed, when one considers the clinical evidence in relation to a careful histologic study of a large series of operative cases of gastric cancer, he is led to the opinion that, in all probability, very few cases of gastric cancer
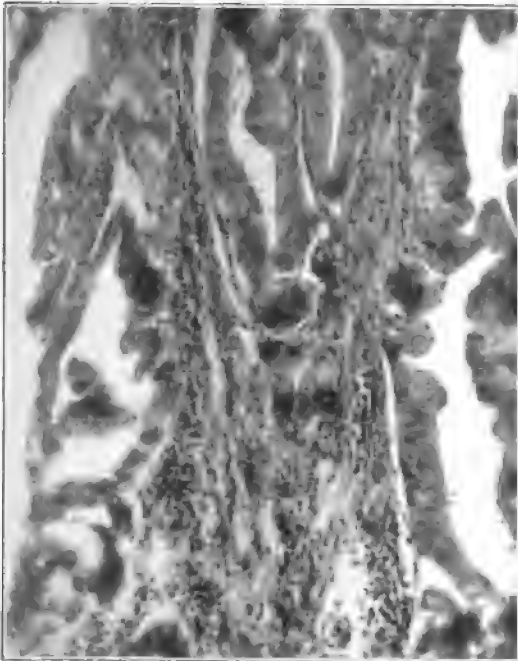
Fig. 73.—Case 12. One-hundred-diameter magnification of section from papillomatous cancer of pylorus.

exist which have not taken their origin at the site of a previous ulcerative lesion of the mucosa. It is only in rare instances—not more than four or five in our entire series—in which there appears a rapidly growing, fungating papillomatous cancer of the pylorus in which no previous ulcerative lesion is suggested. It must be remembered that, even in these, a small chronic ulcer of the pylorus may have been literally covered in by the rapidly growing mucosa. Such a case as this is our Case 12 (52034). (See Fig. 73.)

TABLE I.—ANALYSIS OF CASES IN WHICH SPECIMENS INCLUDED THE SITE OF GASTRIC ULCER OR CARCINOMA. CASES OPERATED ON

	Ulcer	Group 1 (?) Ulcer —Ca.?	Group 1 Ulcer + Early Ca.	Group 2 Ulcer + Adv. Ca.	Group 3 Ulcer? + Cancer.
TOTAL NUMBER.....	170	19 (4.8^c_c)	63 (15.8^c_c)	147 (36.8^c_c)	170 (42.6^c_c)
Average age at operation..	43	51	50	50.9	54.7
Percentage of cases giving chronic history.........	..	(58.0^c_c)	(8.5^c_c)	(70.7^c_c)	(48.8^c_c)
Average number of years of chronic history......	..	9.1	9.0	11.1	13.2
Percentage of cases giving severe recent history...	..	67.0^c_c	82.5^c_c	89.0^c_o	90.6^c_c
Average number of months of acute history.......	..	2.5	4.5	5.0	6.0

Table I contains an analysis of the cases of this series operated on. In the first column are grouped 170 cases of gastric ulcer which are given for purposes of comparison. It will be noted that the average age at operation of these patients was forty-three years, while the average age at operation of the patients with positive ulcer and questionable early or advanced cancer (Groups 1 (?), 1, and 2) was approximately fifty years. At the same time the average age of the 170 patients in the tissues of whom there was undoubted cancer with incomplete evidence of previous ulcer (Group 3) was 54.7 years. These clinical data, so far as they go, are in harmony with the pathologic findings that gastric ulcer first develops and cancer is implanted thereon, and that, after the latter disease proceeds, it obliterates the evidence of previous ulcer.

When one remembers the numerous instances of advanced gastric cancer which have given no symptoms until within a period of a few weeks prior to death, he is struck with the high percentage of cases (between 70 and 80 per cent.) (Groups 1 (?), 1, and 2) which gave a history suggesting gastric ulcer and extending over a period averaging from nine years in the early cases to eleven years in the advanced cases. Group 3 shows that only 48.8 per cent. of the cases in which previous ulceration was questionable gave a history of long previous gastric ulcer, though of the cases which did give a history the average period of symptoms was over thirteen years.

Sixty-seven per cent. of the cases of ulcer with questionable carcinoma gave histories suggesting carcinoma extending over an average period of two and a half months; 82.5 per cent. of the cases of ulcer with early carcinoma gave histories suggesting gastric cancer extending over an average period of four and a half months; 89 per cent. of the cases of ulcer with advanced carcinoma (Group 3) gave histories suggestive of cancer extending over an average period of five months; 90.6 per cent. of the cases of cancer with questionable ulcer gave a history suggestive of cancer extending over an average period of six months. These data are interesting in relation to a study of 566 consecutively operated and pathologically demonstrated cases of cancer of the stomach in our Clinic (Smithies*).

TABLE II.—ANALYSIS OF CASES IN WHICH SPECIMENS INCLUDED THE SITE OF GASTRIC ULCER OR CARCINOMA. AUTOPSY CASES

	Ulcer	Group 1 (?) Ulcer + Ca.?	Group 1 Ulcer + Early Ca.	Group 2 Ulcer + Adv. Ca.	Group 3 Ulcer ? + Cancer.
TOTAL NUMBER......	15	1 (2.2%)	....	7 (15.2%)	38 (82.6%)
Average age at operation or autopsy.............	..	57.0	....	54.7	54.1
Percentage of cases giving chronic history.........	..	....	....	....	50.0%
Average number of years of chronic history	..	9.0	....	4.0	7.9
Percentage of cases giving severe recent history....	..	....	....	....	76.0%
Average number of months of acute history........	..	1.0	....	2.8	4.5

The analysis of the cases from which the specimens were obtained at autopsy (see Table II) gives little significant data, since the cases are too few. It is worthy of note, however, that the average age at operation of these cases was practically the same in Group 3 as in the cases operated on of Group 3, while the average number of years of precedent ulcer history and the average number of months of cancer history are both shorter than the similar periods for the cases operated on of Group 3. These figures, so far as they go, would suggest that there is a small group of cases

* Jour. Amer. Med. Assoc., 1913, lxi, 1792–1799.

of rapidly developing cancer which symptomatically are without evidence of precedent ulcer.

TABLE III.—SUMMARY OF SUBSEQUENT HISTORIES (INQUIRIES DATED FEBRUARY 1, 1913)

GROUP 1 (?).—ULCER + CARCINOMA (?)

Total cases reported	5
Alive	1
Condition good	1
Average months after operation	7
Dead	4
Under thirty days	0
Average months after operation	27.5

GROUP 1.—ULCER + EARLY CARCINOMA

Total cases reported	41
Alive	23
Condition good	16
Condition fair	6
Condition bad	1
Average months after operation	30
Dead	18
Under thirty days	6
Average months after operation for remaining 12	28

GROUP 2.—CANCER ON ULCER. BASE FREE

Total cases reported	94
Alive	35
Condition good	22
Condition fair	4
Condition bad	9
Average months after operation	34
Dead	59
Under thirty days	18
Average months after operation for remaining 41	14

GROUP 3.—ULCER (?) + CARCINOMA

Total cases reported	97
Alive	19
Condition good	12
Condition fair	2
Condition bad	5
Average months after operation	24
Dead	78
Under thirty days	34
Average months after operation for remaining 44	14

The examination of Table III, which contains a summary of the subsequent histories so far as they have been obtained in these cases, shows the following:

Of the 19 patients in Group 1 (?), 1 is reported in good condition seven months after operation and 4 are reported dead, an

average period of twenty-seven and a half months after operation. One of these patients died of typhoid fever, the other three of cancer.

Of the 41 patients in Group 1 from whom subsequent histories have been received, 23 are reported alive; 16 of these were in good condition, 6 in fair condition, and 1 in bad condition, an average of thirty months after operation; 6 died in less than thirty days after operation, and 12 were reported dead, an average period of twenty-eight months after the operation. So far as we have been able to determine, all these patients died of cancer.

Of the 94 patients in Group 2 of whom subsequent histories have been received, 35 are reported alive, 22 in good condition, 4 in fair condition, and 9 in bad condition, an average of thirty-four months after operation; 18 of these patients died in less than thirty days after operation and 41 more were reported dead, all except 1 apparently of recurrent cancer in an average period of fourteen months after operation.

Of the 97 patients in Group 3 of whom subsequent histories were received, 19 were reported alive, 12 in good condition, 2 in fair condition, and 5 in bad condition in an average of twenty-four months after operation; 34 died in less than thirty days after operation and 44 others were reported dead on an average of fourteen months after operation. An analytic study of the clinical data on these cases will be presented later by Graham and Eusterman.

SUMMARY

1. Of the 399 cases of gastric cancer from which the tissue containing the primary lesion was resected in the Mayo Clinic, 4.8 per cent. show ulcers with doubtful cancer in the border (Group 1 (?)), 15.8 per cent. show ulcer with positive early cancer in the borders only of the lesion (Group 1), 36.8 per cent. show ulcers with advanced cancer (Group 2), while 42.6 per cent. of the cases show cancer in which the evidence of previous ulcer formation is doubtful (Group 3).

2. Of the 46 cases of gastric cancer from which the tissue con-

taining the primary lesion was obtained at autopsy, 1 case (2.2 per cent.) shows an ulcer with doubtful cancer (Group 1 (?)), 7 cases (15 per cent.) show ulcer with advanced cancer (Group 2), while in 38 cases (82 per cent.) the evidence of ulcer previous to cancer formation is doubtful.

3. The clinical and pathologic data in relation to the development of gastric cancer or gastric ulcer are in close agreement: (a) with regard to the average age at operation; (b) with regard to the average period of previous history suggestive of ulcer; and (c) with regard to the average number of months of acute history. Such an agreement of data from two independent studies of this series of cases is not accidental.

4. It seems probable from a careful study of the clinical and pathologic evidence of this series of cases that gastric cancer rarely develops except at the site of a previous ulcerative lesion of the mucosa.

IV. STUDIES IN THE PATHOLOGY OF EARLY GASTRIC CARCINOMA *

LOUIS B. WILSON

We are still far from either an explanation of the primary cause of or a demonstration of the initial cell changes in gastric carcinoma. Much of our study of cancer in the past has been focused on the morphology of the gross lesion. The term "cancer" still suggests to most minds a large mass, though a moment's consideration compels the agreement that every cancer must start with a few cells. The finding of these cells and the determination of their malignant character is one of the most difficult tasks of the pathologist who is making a diagnosis while the surgeon waits. Fortunately, however, he is not called upon to search for minute cancers except where a gross lesion already exists. Were he to attempt to find beginning cancer in the stomach in which no gross lesion is present, he would have a yet more difficult task. DeWitt[1] has shown that the secreting surface of a single pyloric gland of the human stomach measures over 100 square millimeters in area, and that there are from 125 to 140 such glands opening on each square millimeter of the surface of the mucous membrane of the human pylorus. She calculates from this that each square millimeter of the surface of the mucous membrane of the pylorus represents approximately 13,500 square millimeters of secreting glandular surface. It will thus be seen that if one were to set out to find the few cells showing the first changes indicating carcinoma, and were not guided by any associated gross lesions, he would need to search with a microscope over an area more than 10,000 times greater than the

exposed surface of the stomach, or a space of over 5000 square feet. The hopelessness of such a needle-in-the-haystack search would prevent any one undertaking it. It is possible that gastric cancers do originate in gastric mucosa which gives no grossly visible sign of irritation, and it is conceivable that some one may some time find such a cancer, though it will no doubt be accidental and on autopsy material. We have learned that the most likely place in which to find early gastric cancer is in the border of a chronic ulcer in a patient of cancer age whose history has caused the clinician to make a diagnosis of gastric ulcer and the surgeon to excise or resect a portion of the stomach containing the lesion. The whole question then turns upon our ability to determine microscopically the presence of early cancer in association with non-cancerous lesions; or, in other words, to differentiate the early cell changes associated with malignancy from the late cell changes in non-cancerous lesions. This necessitates a comparison of normal embryonic and adult mucosa, and of acutely and chronically irritated mucosa, with the cells in the mucosa showing early cancerous change. As a basis for such a comparison I have thought it desirable to bring together in a brief review those results of the more recent studies in the histogenesis, histology, and physiology of the gastric mucosa which seem to be related to the site and morphology of the cell changes in early gastric carcinoma.

HISTOGENESIS

The careful study of the embryology of the stomach from the histogenic standpoint, brilliantly begun by Sewall[2] and carried forward by many others, has fairly definitely settled the histogenesis of the gastric mucosa in detail.

All investigators are agreed that embryologically the gastric glands begin as downgrowths of the endoderm; that all the cells lining the foveolæ or pits are of this origin, and that most, if not all, of the cells lining the gland tubules are from the same source.

Kirk,[3] in describing the development of the glands of the pig, says: "At no stage does the epithelium acquire stratification except in the pars œsophagea. All the cells reach from the basement-

membrane to the surface.   There are no basal cells in the sense of cells which are shut off from the gastric lumen by higher cells."

The formation of new gastric glands continues after birth. Toldt[4] estimated that in the gastric mucosa of the child ten years of age the total number of gland outgrowths of the stomach is approximately ten times what it is at birth, and that the number of gland tubules is increased again almost ten-fold in the stomach of the adult, in which he estimated the total number as 25,179,000.

Concerning the method of renewal of gastric epithelium in the adult, Bensley,[5] from a study of adult human material, makes the following important observation:

"The mitoses seem to be entirely confined to the cells of the bottom of the foveolæ and adjacent portions of the gland tubule. I have not observed a single instance of cell division in surface epithelium nor in the cells at the bottom of the gland, although the cells near the foveola may divide even when they contain a good deal of secretion.   The great mitotic activity at the juncture of the gland and foveolæ, as well as the gradual transition from this point in both directions, led me to believe that this is the site of the reproduction of both the surface epithelium and glandular epithelium, both of which are probably replaced when lost by a gradual migration of cells from the point at which they are produced."

Summing up our knowledge of the normal development of the gastric mucous membrane as related to epithelial overgrowths, we note the following:

1. In this tissue we have epithelial cells which, though all developed from a single layer of embryonic endoderm, yet differentiate into cells of three definite morphologic types—the ovoid parietal cells, the pyramidal chief cells, and the cylindric surface cells, associated with three definite physiologic functions, the formation of acid, of zymogen, and of mucus.

2. For the replacement of destroyed epithelium new cells are supplied by fission of already differentiated cells, a process which takes place most actively at the juncture of the foveola and the neck of the gland.

3. The formation of new gastric gland tubules continues into adult life. This takes place by active epithelial downgrowth from the bottom of the foveolæ or gastric pits.

HISTOLOGY

Surface and Foveolæ.—Bensley[6] says:

"The whole of the surface and walls of the foveolæ gastricæ are covered with a simple cylindric epithelium, mucigenous in function and uniform in type throughout the stomach. The epithelium of the foveolæ gastricæ is similar to that of the free surface."

Fundic Glands.—The fundic zone extends from within about 4 cm. of the esophagus to within about 5 cm. of the pylorus. The glands of the fundus are more or less slightly irregularly curved, branched tubules. The tubular portion of the gland proper consists of two portions, the narrow neck opening into the foveola and the body extending to the base of the gland. The cylindric cells lining the foveolæ pass by a gradual transition into the cells of the neck of the gland tubule.

Harvey[7] has shown that there is no gradual transition from the chief cells of the neck to the chief cells of the body, but that there is an abrupt change. The parietal cells occur in all parts of the gland, although they may be found in the greatest numbers in the neck of the gland. In the foveolæ only an occasional parietal cell may be seen. Mitotic divisions are extremely rare among the parietal cells. Parietal cells are probably the sole source of hydrochloric acid in gastric juice.

Harvey,[7] in studying canine material, notes that a few parietal cells react to chrome salt fixation and subsequent staining very much as do the chromaffin cells in the suprarenal gland and various parts of the sympathetic system.

Pyloric Glands.—The glands of the pylorus are much less closely set than in the fundus.

"The foveolæ into which they open are narrow. They rapidly diminish in diameter, to become narrow tubes which branch as they descend in the mucous membrane. Into the bottoms of

these foveolar branches open the pyloric glands. These are composed of a varying number of branching, wavy tubules into which open short, pear-shaped acini" (Bensley[6]).

Morphologically and physiologically the cells in the pyloric glands are regarded by Bensley[8] and Harvey[7] as equivalents of the mucous chief cells found in the necks of the fundus glands.

Cardiac Glands.—The cardiac glands may extend from a point 3 mm. above the termination of the esophageal epithelium to a point 4 cm. below the termination of the esophageal epithelium. Bensley's[5] conclusions from a study of the histology of these glands are as follows:

"1. Cardiac glands are mucous glands and are connected with the mucigenous epithelium of the surface by a transition, the middle point of which is formed by actively dividing cells containing little mucin, which occur at the deeper constricted ends of the foveolar depressions."

"2. The cardiac gland cells are fundamentally different from the chief cells of the body of the fundus glands, inasmuch as the latter give none of the staining reactions of mucin, but, on the contrary, contain two characteristic substances which are phases in the elaboration of their secretion, *i. e.*, zymogen granules and prozymogen."

"3. The cardiac gland cells are closely related to the mucous chief cells of the neck of the fundus gland and to the pyloric gland cells."

"4. The cardiac glands are decadent or retrogressive structures derived from fundus glands by the disappearance of their more highly specialized cellular constituents, the zymogenic chief cells and the parietal cells."

"In the case of the human stomach, in the cardiac glands of which both parietal cells and ferment-forming chief cells are present in small numbers, the distinction between cardiac glands and fundus glands might be dispensed with altogether."

'14—10

PHYSIOLOGY

It is beyond the limits of the present review to go fully into the physiology of the gastric secretions. Our present knowledge, however, of the secretions of the various portions of the gastric mucous membrane as apparently significantly related to the histology of gastric cancer may be summarized as follows:

Pawlow[9] seems to have shown that the true physiologic function of the surface epithelium of the stomach is the secretion of large quantities of mucus, which, by the dilution of noxious substances or the formation of inert chemical combinations therewith, prevent their deleterious action on the more important elements of the underlying glands.

The gastric glands of the cardiac zone secrete only mucus (Bensley[5]) with an alkaline reaction (Greenwood[10]).

Of the glands of the fundic zone, the chief cells furnish the digestive enzymes, pepsin and rennin, and the parietals some chlorid of an organic base which, on reaching the mouth of the gland, in some way yields free HCl, though the parietal cells themselves, as shown by indicator stains, have an alkaline reaction (Harvey and Bensley[11]). The degree of acidity of the gastric juice as secreted under relatively normal irritation is remarkably constant, the wide variations in the mixed juice being due to different degrees of neutralization of the acid by contact with the alkaline mucous membrane or its secretion of alkaline mucus (Pawlow[9]).

Clowes and Jeffcot[12] have shown that there nearly always is an increase in the fixed chlorids of the gastric contents when free hydrochloric acid is absent.

With regard to the function of the pyloric glands, there is considerable disagreement. Starling[13] says: "A pyloric culdesac yields a secretion which is neutral or slightly alkaline, but which contains pepsin." Bensley[6] says: "The theory of Heidenhain that the cells of the pyloric glands are pepsin-forming elements similar in character to the chief cells of the body of the fundic glands has been shown to be incorrect. . . . . Morpho-

logically and physiologically they are the equivalents of the mucous chief cells found in the necks of the fundic glands."

While the latter view is probably correct of the pyloric glands under normal conditions, the observation of Harvey[7] that, at least in the fundic glands of the dog under pathologic conditions, the functions of zymogen and mucin-formation seem to be interchangeably assumed by the same cell, offers a possible explanation of the apparent discrepancies between different observers.

A number of writers have noted the presence of small amounts of glycogen in gastric epithelium in the presence of scirrhous and adenomatous cancer. Lubarsch,[14] who has made a most careful study of the pathologic significance of glycogen, does not consider it important in relation to malignancy of neoplasms.

PATHOLOGIC CELL CHANGES IN NON-CANCEROUS LESIONS

Cohnheim,[15] in a study of the histology of specimens from cases of hyperacidity, notes that the epithelial changes consist mainly of a disappearance of the principal cells and a proliferation of the parietal cells.

Harvey[7] has studied simple forms of pathologic change in the stomach occurring in the gastric glands of dogs after gastro-enterostomy. He notes that after gastro-enterostomy the mucous membrane within 7 mm. of the line of operation undergoes the following changes:

"The body chief cells, which are normally ferment-forming, become transformed into mucus-forming cells. This is a gradual process, beginning immediately after the operation at the line of suture and extending radially about the anastomosis, reaching its maximum extent of 7 mm. about three weeks after the operation. After one month a reverse transformation commences and the same cells again become ferment cells. This process is completed by six and a half months after operation. After that the gastric glands next to the duodenal glands at the anastomosis do not differ materially from those remote from it. This is a transformation of cells, not a replacement. Cells were found containing both mucus and zymogen. Since cells very highly specialized may

undergo such transformations, the term 'specific' must be applied to them with care, and only after prolonged study by the experimental method."

Hauser[16] was the first to show that in gastric ulcer new tubular glands are formed which are lined by cylindric cells and may undergo cystic dilatation.

MacCarty,[17] in a study of the histology of human gastric ulcer, noted that:

"In the smallest ulcer the bases of the cells rest regularly on a basement-membrane and do not penetrate it. The relative proportion between the nucleus and protoplasm is that of a differentiated cell, and is about one to three or one to four. The nuclei take the stain densely and are either oval or round, and vary in size and shape between the normal limits of normal gastric gland nuclei, depending on the plane in which they are cut. They are regular in shape and size. In the border of an ulcer which shows a more marked reaction to the irritant the same picture may be seen accompanied by more extensive hyperplasia and increase in the relative proportion of the size of the nucleus to protoplasm. The nuclei stain less densely. In this condition the line of demarcation between the stroma and the gland is usually not so regular. The glands may be, and often are, distended and distorted."

PATHOLOGIC CELL CHANGES IN GASTRIC CANCER

One of the earliest descriptions of the tissue changes at the beginning of gastric cancer is that by Waldeyer (quoted by Welch[18]), who described in detail the origin of gastric cancer from the gastric tubules. According to his description, a group of gastric tubules, 10 to 20 in number, send prolongations downward into the submucous coat. These tubular prolongations are filled with proliferating epithelial cells which make their way into the lymphatic spaces of the surrounding tissue and give origin to the cells in the cancerous alveoli.

Fenwick and Fenwick[19] thus describe the histology of early gastric cancer:

"The earliest signs of a departure from the normal consist of
an active proliferation of the epithelium of a small group of glands,
which leads to distention of the tubules with cells of various shapes
and sizes, obliteration of their lumina, and a marked alteration
of their outlines.   Many of the newly formed cells exhibit particles
of brownish black pigment, and the oxyntic cells of the neighbor-
ing glands are often affected in a similar manner.   The epithelial
overgrowth soon gives rise to elongation, twisting, and distortion
of the tubules, which cause them to appear branched or racemose,
while the ducts become choked with débris and their columnar
cells filled with mucus.   Up to this period the morbid process
closely resembles an adenoma; but it now displays its malignant
character by the rupture of the basement-membranes of the
affected glands and escape of the epithelium, which continues to
penetrate the surrounding connective tissue in the form of branch-
ing columns similar in appearance to the peptic glands, but de-
void of a membrana propria."

MacCarty and the writer,[20] in a study of gastric ulcer and
gastric carcinoma, noted that, deep in the overhanging borders
of chronic gastric ulcers in which the mucosa is proliferating,
many groups of epithelial cells are exhibiting all stages of aberrant
proliferation, with infiltration of the surrounding tissue.

From the preceding review it is obvious that much yet re-
mains to be learned concerning the morbid histology, and espe-
cially concerning the finer cell changes in early gastric carcinoma.
With the hope of perhaps being able to add somewhat to the data
by which we may more confidently diagnose early malignant
changes in the stomach I have recently made a study of thin
serial paraffin sections from specimens of early gastric carcinoma
removed at operation in the Mayo Clinic.   The lesions of these
specimens involve the gastric glands of the pyloric zone, though
many of them include also glands from the fundic zone.   Without
going at length into a discussion of the details of this study, I may
state briefly that the following observations have been made:

1. One of the most commonly noted changes in chronic ulcers
which show early carcinoma is cystic dilatation of the bases of the

glands. These cysts in carcinomatous specimens are not lined with flattened epithelium, as one would expect in cysts due to blocking of the gland tubule, but they are lined with a single layer of large columnar cells, the nuclei of which are sometimes crescentic, but more frequently rounded, showing that the cells which are apparently secreting mucus are yet able to empty themselves readily. This condition is shown in Fig. 74, in which the nuclei are crescentic, and in Fig. 75, in which the nuclei are spheric. Many such cells show mitotic figures, an evidence that they are proliferating, a condition which is further shown by the greatly
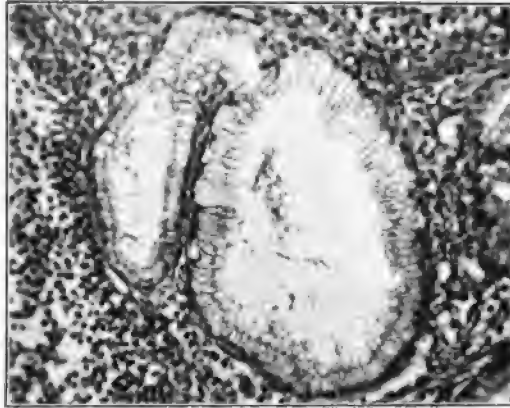
Fig. 74.—(94647.) High-power magnification of section across cyst of pyloric gland in early gastric cancer. Columnar cells filled with mucin; crescentic nuclei.

increased number of cells in a transverse section of a tubule. The fact that the epithelial cells of the gastric tubules may so markedly proliferate without forming superimposed layers is in consonance with the well-established observation that embryologically the epithelium of the gastric glands is always in a single layer. In view of the fact that a somewhat similar proliferation of the cylindric cells of the gastric glands is seen also in the mucosa surrounding the borders of chronic ulcers in which there is no other evidence of malignancy, one must hesitate to diagnose carcinoma from such a condition alone.

2. Apparently the next step in the changes in the epithelium of the tubules in early gastric cancer is an increase in the number of layers of the lining cells. This seems to occur most frequently in the necks of the gland tubules. Associated with the super-imposition of cells are a change from the pyramidal or cylindric form to rhombohedral forms, a great increase in the size and ir-regularity of the nuclei, and a marked increase in their staining affinity. This is well shown in Fig. 76. The piling-up process may become quite extensive without the obliteration of the lumen, as is shown in Fig. 77.
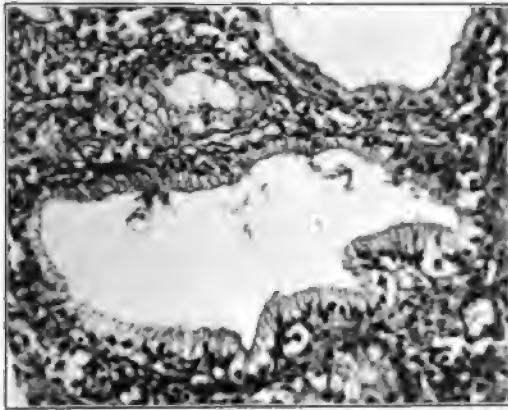
Fig. 75.—(94647.)   Same tissue as in Fig. 74, but with cells freely discharging their mucin; spheric nuclei.

In many instances the cells which have been crowded away from their supply of nutrition in the vessels early show degenerative changes. These changes consist in an obliteration of the outlines of the cytoplasm and a destruction of its reticular network, a lessening of the affinity of the nuclei for stains, and sometimes a mucoid degeneration.

The above-described condition is the earliest which may be certainly diagnosed carcinoma.

3. The formation of mucin by the gland cells of the pylorus, if one may judge by its staining reactions, goes on in an appar-

ently normal manner, but in greatly increased amount, even after
cell proliferation is most marked.   In a large percentage of cases,
however, a change occurs in the mucin which materially alters its
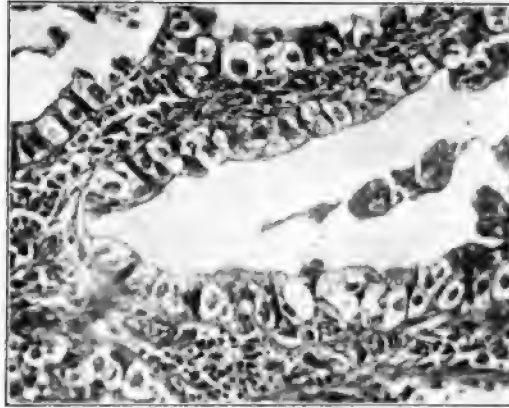
Fig. 76.—(80863.)   Similar to Fig. 75, but with beginning multiplication of layers of epithelium.
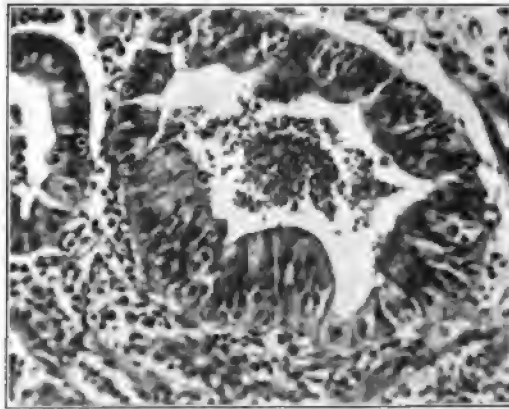
Fig. 77.—(53784.)   Similar to Fig. 76, but with marked piling of epithelium.

staining reaction.   After formaldehyd or chrome salt fixation,
one frequently sees cells containing small droplets which, with
Delafield's hematoxylin, stain an intense clear dark blue, with no

shading to brown or black like that of the near-by nuclei.   These
masses of mucin may fill the entire cell, in which case they show
a reticulated structure made up of fine fibrils (Fig. 78).   They are
much the most numerous in the mucous cells of the pyloric gland
tubules, but they are found also in the mucous cells of the foveolæ
and of the surface epithelium.   In a few instances they are present
in gland tubules in the fundic region in such a situation and of
such a shape as to make it almost certain that they are within
parietal cells.   They apparently also occur within the zymogen
cells of the fundic tubules.
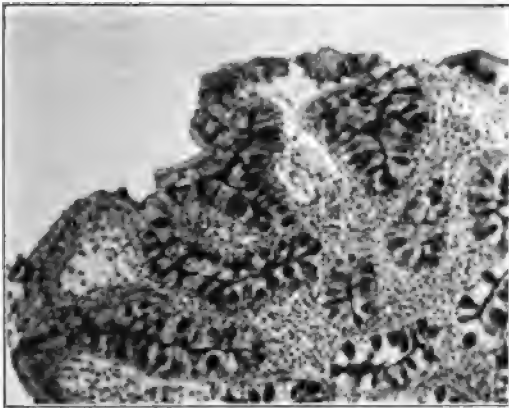
Fig. 78.—(97051.)   Densely staining mucin within columnar cells.

This mucigenous degeneration of the cells may go on to such
an extent as completely to destroy all the cell outlines within a
cross-section of a tubule.   It is probably the beginning of mucoid
cancer, though, from its frequency, it would seem improbable that
all cases showing a primary degeneration of a few cells later be-
come grossly mucoid.   The intense staining reaction resembling
that marking the presence of a carbonate would suggest that the
substance is strongly alkaline, though mucin normally is neutral
or feebly alkaline.

4. Occasionally, though rarely, the proliferating tubules, in-

stead of showing a multiplicity of layers of epithelial cells, and instead of becoming greatly enlarged in transverse diameter, seem to elongate and coil up upon themselves within walls of fibrous connective tissue, producing adenomatous-like structures.

5. Not infrequently, in the interstices of the fibrous tissue at the margins of chronic ulcers under the borders of the overhanging mucosa, are found groups of cells which may or may not surround any central opening, but which give one the impression of being isolated and pressed upon externally by the overgrowth of fibrous
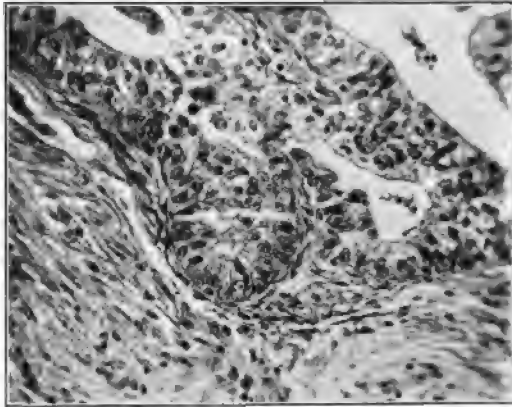
Fig. 79.—(29584.) Similar to Fig. 77, but with infiltration of stroma.

tissue.   It is difficult to determine the complete occlusion or isolation of these groups of cells without careful reconstructions of serial sections.   The cells in these groups often show by their mitoses and their metachromatic staining that they are actively proliferating.   They certainly have all the appearances of groups of cells which have penetrated into the muscularis in more advanced gastric cancer.   It is hardly probable that they are advancing tips of new gastric glands.

6. In some specimens the overgrowth of the epithelium lining the necks of the glands seems to result in an increased twisting of

the gland tubule. This, of course, can be followed out only in serial sections.

7. The proliferation of endothelium within the gastric glands may go on until the tubule is packed completely full of cells (Fig. 79). When this occurs, there is nearly always infiltration of the epithelial cells into the surrounding connective tissue. This last stage seems to be the only positive criterion by which some pathologists are willing to diagnose gastric cancer. To those of us who are seeing many cases in their early stages and following up the patient's history subsequent to operation, such pictures present only evidence of advanced, rather than early, cancer. If the surgeon waits for the presence of extensive infiltration in gastric carcinoma before operating, he may hope to give the patient only a slightly more comfortable death by a palliative procedure.

PRACTICAL CONSIDERATIONS

1. Although the surface of the secreting cells of the gastric glands is of enormous extent, and carcinoma theoretically may start in any minute group of such cells, or even in a single cell, yet one looks for early carcinoma only in the presence of gross lesions. These lesions are ulcerative and are found ordinarily in the pyloric zone or, if in the fundic zone, more usually on the lesser curvature in the stomachs of patients most frequently between thirty and sixty years of age, who, in a high percentage of cases, have given a history suggesting chronic gastric ulcer. The absence of such a history, especially as indicated by pain, is, however, very common, even in cases in which the pathologic condition proves beyond a doubt that a gastric ulcer must have been present for years.

2. Usually at the most thickened side of such an ulcer, in the base of the overhanging mucous border, either at the necks of the glands or in their terminal subdivisions, are to be found the earliest evidences of malignant change.

3. When the histologic pictures above described are present, the pathologist is warranted in making a diagnosis of carcinoma before there is infiltration of the interglandular tissue with epi-

RADIOLOGIC SIGNS OF DUODENAL ULCER
With Special Reference to Gastric Hyperperistalsis *

RUSSELL D. CARMAN

While increased gastric peristalsis has been commonly listed among the radiologic signs of duodenal ulcer, it has not received the emphasis which it deserves as an independent diagnostic indication, and no serious effort has been made to estimate its value relative to other signs and thus to show its specific importance. More often it has been casually remarked as a mere feature of hypermotility. Foreign radiographers have, in a general way, remarked its frequency, but without going into large figures or refined details. In this country attention has been almost wholly directed to other signs. My own experience with this sign has been so strongly confirmatory to its high importance that I venture to present herewith brief statistics of 198 cases of duodenal ulcer operatively confirmed, showing the percentage in which hyperperistalsis was noted.

The establishment in recent years of duodenal ulcer as an anatomicopathologic entity and the frequency of its incidence have led to rapidly increasing knowledge of this condition. In the past ulcer of the duodenum has no doubt been confounded with ulcer at the pyloric end of the stomach, partly because of the assumption that any ulcer found in the vicinity of the pylorus must necessarily be gastric, and partly because of the difficulty of determining the exact site of the pylorus. In 1907 W. J. Mayo ("Ann. Surg.," June, 1907, p. 811) called attention to the pyloric vein as a landmark corresponding accurately to the pyloric sphincter. More care-

ful determination of the pyloric site has resulted in finding that the ratio of frequency between duodenal and gastric ulcer is far greater than has been supposed, being now variously stated as three and even four to one.

Notwithstanding the constantly growing mass of convincing statistics, many clinicians, and especially a few gastro-enterologists of this country and continental Europe, are on record as claiming that duodenal ulcer is a lesion which rarely occurs. Their inability to recognize its frequency is probably due, as W. J. Mayo states, to the presence of the abdominal wall.

Speaking from a radiologic point of view, I might say that during the last year only have I come to realize the frequency of this condition through following cases to operation and looking into the abdominal cavity with the surgeon. I should certainly recommend this procedure to those who are skeptical, because a large number of the patients treated for "chronic dyspepsia" have duodenal ulcer.

At present the diagnosis of duodenal ulcer depends chiefly on the anamnesis. Conceding that the history is diagnostic with a relatively small percentage of exceptions, the tendency is to supplement this with physical methods, in which error due to the personal equations of the observer and patient can be more or less eliminated. Of these adjuncts the Roentgen ray is the more important.

RADIOLOGIC SIGNS

The roentgenologic indications of duodenal ulcer, which have been frequently catalogued by various observers during the past two years, may be divided into major and minor signs. The major signs are:

1. Gastric hyperperistalsis.

2. A residue in the stomach (sometimes in the duodenum) after six hours if there be obstruction from scar contraction.

3. A diverticulum of perforating ulcer.

The minor signs include:

1. Gastric hypermotility with early free opening of the pylorus and speedy clearance of the stomach.

2. Gastric hypertonus.

3. Irregularities in the outline of the cap or bulb or of the duodenum.

4. Lagging of bismuth in the duodenum.

5. Pressure-tender point over the duodenum.

6. Spasms of the stomach, such as hour-glass or slowly traveling incisura.

The technic by which these signs may be elicited is varied.
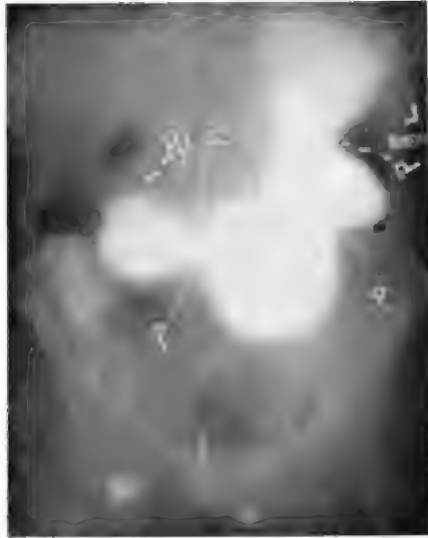
Fig. 80.—The white area is the bismuth-filled stomach. The indentations, marked *P*, are peristaltic waves, the depth of which shows the vigor of contraction. *Pyl.*, Pylorus. In this case there was marked obstruction, as shown by a residue of three-fourths of the bismuth meal after six hours. The extreme exaggeration of the peristalsis is due in part to this obstruction. At operation a large, irregular ulcer of the duodenum was found. Lumen of duodenum reduced to size of a lead-pencil at the point of obstruction.

One of the most satisfactory is the double-meal method. Our present routine is as follows:

1. Purgation with castor oil, given the evening prior to examination.

2. Two ounces of chemically pure barium sulphate in a portion of breakfast cereal given to the patient the next morning.

3. Fluoroscopic screen examination six hours later, during

which the patient is first given 2 ounces of bismuth subcarbonate in 6 ounces of water, then 2 ounces of bismuth subcarbonate in 16 ounces of potato-starch pap.

4. Plates made at once after screen examination, and subsequently at intervals if desired, in either the prone or standing position, preferably the latter.

HYPERPERISTALSIS

Gastric hyperperistalsis has long been included among the Roentgen-ray indications of duodenal ulcer, but has usually been mentioned as incident to hypermotility with early clearance of the stomach, which latter sign has been given greater prominence. While increased peristaltic action may sometimes promote an early evacuation of the stomach, there is no fixed relation between the two.

Whenever the combined screen and plate method of examination is used, peristaltic exaggeration in duodenal ulcer is readily discoverable, occurs in a large proportion of cases, and has a high diagnostic value regardless of the time of gastric clearance.

The intensity of peristaltic vigor, as we have noted it in this condition, using the technic previously described, varies from a slight exaggeration of wave-depth to an almost tumultuous energy of contraction. So extreme is the latter in the obstructive cases that the stomach is nearly segmented by the opposed waves and resembles a row of balls. The peristaltic contractions on the lesser curvature participate in the tempest. Normally traversing only a small portion of the lesser curvature and deepest at their termination, they now seem to cover a wider range and are deep throughout. This symmetry and correspondence of the contractions on both curvatures are a distinctive feature. The waves are increased not only in depth, but also to some extent in frequency, so that three or four pairs may be seen in progress at once, whereas normally, using the media mentioned, only one or two very superficial pairs are seen.

This exaggeration of gastric peristalsis does not seem to be related to hyperacidity, because it has been noted in many of the

'14—11

cases of ulcer with moderate or low acidity. On the other hand, cases of gastric ulcer and appendicitis (the latter especially) with high acidity have not shown this phenomenon. Neither does it appear to be merely compensatory to obstruction from stenosis of the duodenum, since we have seen it repeatedly where obstruction did not exist in sufficient degree to produce a six-hour residue or to be evident at operation.
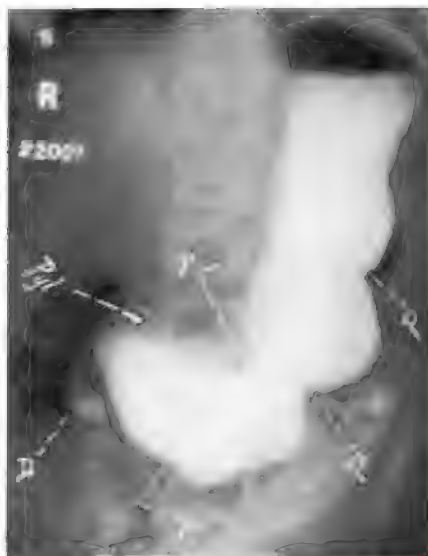
Fig. 81.—Deep peristaltic waves, indicated by *P*; *D* marks bismuth in duodenum; *Pyl*, pylorus. One-half the bismuth meal was retained in the stomach after six hours. Operation showed obstructing ulcer of the duodenum.

It has been my observation that stenotic lesions on the gastric side of the pylorus are rarely accompanied by gastric hyperperistalsis. Even if the peristalsis be greater than normal, it is not likely to be bilateral, but will show its activity chiefly on the greater curvature. Here one is more likely also to see antiperistalsis, as I have in several cases. I have never seen antiperistalsis in duodenal irritation, even with obstruction.

The exaggerated peristalsis which may be evoked by massage

of the epigastrium differs from the hyperperistalsis of duodenal ulcer in the fact that the former subsides very quickly after manipulation ceases. The hyperperistalsis of duodenal ulcer requires no external stimulation to induce it. During and immediately after the ingestion of the bismuth water peristalsis often seems rather marked, but this soon subsides. After filling the stomach with the bismuth pap, on the contrary, the institution of peristalsis

Fig. 82.—Same case as in Fig. 81. Roentgenogram made immediately after that shown in Fig. 81. *D*, Duodenum; *Pyl.*, pylorus. Note absence of peristaltic indentations. This case illustrates the intermittency of the peristalsis.

is quite commonly delayed for some minutes, reaching its maximum vigor still later. The hyperperistalsis of duodenal ulcer is quite commonly of an intermittent character. It may be noted on the screen, but not seen on the plate, or vice versâ. Hence observation should be prolonged until this sign has had time to appear.

The degree of peristaltic vigor is apparently influenced by the character of the opaque meal. The commercial condensed milks, which contain butter-fat, markedly depress peristalsis. Fermented

whole milk, buttermilk, and potato-starch pap are admirable media and do not adversely affect peristaltic action. Bismuth oxychlorid is believed to produce more vigorous action than does the subcarbonate. This is also true of barium sulphate. It has also been observed that in plates made with the patient prone the peristaltic vigor is more pronounced than in plates made of the same patient when standing. For these reasons one should have a uniform technic, so that comparisons may be on the same basis.

Exaggerated peristalsis above an irritative lesion of the digestive tube has been often observed radiologically and produced experimentally. In duodenal ulcer duodenal irritation must exist as a constant or nearly constant factor. Why, then, is hyperperistalsis not seen constantly? Is its absence in some cases due to psychic influences, such as fright or disgust for the bismuth meal? Is it sometimes delayed in appearance and thus overlooked in a brief examination? Is it because of peculiarities in the distribution of the nerve-supply? Does the situation of the ulcer play a part? All these are problems worthy of investigation.

SIX-HOUR RESIDUE

Of all the radiologic signs of lesions of the digestive tract, the presence, after six hours, of a distinct residue from the barium or bismuth meal is perhaps the most important. The radiologist feels assured that almost without exception such a residue signifies an organic lesion, whether or not all his diagnostic deductions be confirmed. Theoretically, a residue may remain in simple atony, and we have had one case (no operation) in which this was believed to be true; but of our cases with residue which came to operation every one was found to have some condition requiring surgical intervention.

A residue in the stomach from the barium or bismuth meal, six hours after its ingestion, occurs in a large proportion of cases of duodenal ulcer. This is often loosely spoken of as being due to pyloric obstruction, whereas the obstruction is actually in the duodenum and is produced by ulcer—scar contraction. Occasionally there will be found not only a six-hour residue in the stomach,

but also a six-hour residue in the duodenum above the stenosis, thus enhancing its diagnostic value.   A six-hour residue may, however, also be found in the stomach as a result of gastric ulcer or carcinoma or thickening of the pyloric ring.   A six-hour residue in the duodenum may result from bands of adhesions or from the pylorospasm incident to gall-bladder disease.
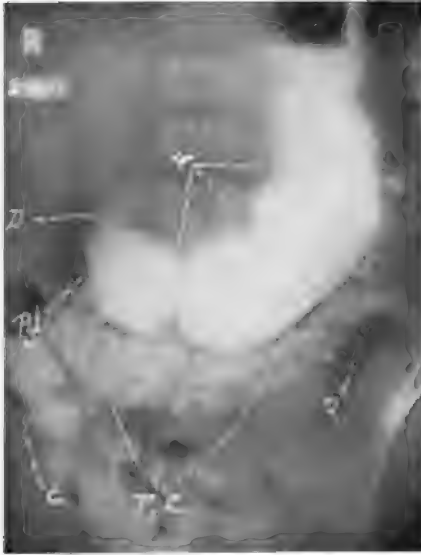
Fig. 83.—*Pyl.*, Pylorus; *D*, duodenum; *P*, peristaltic waves; *C*, cecum; *T. C.*, transverse colon. Vigorous peristalsis was more marked on the screen than on the plate. No obstruction. Operation showed semiperforating duodenal ulcer two inches below pylorus.

DIVERTICULUM

The diverticulum of perforating duodenal ulcer is rather decisively diagnostic when found, but its rarity is shown by the fact that in the 198 cases herein reported only 2 showed this phenomenon, both of which were diagnosed radiologically.

HYPERMOTILITY WITH EARLY CLEARANCE OF THE STOMACH

At the screen examination the bismuth water, immediately after being swallowed, is often seen to flow freely and spontaneously

into the duodenum, sometimes visualizing the latter throughout. When the flow is not spontaneous, slight pressure on the stomach, or, as I have occasionally noted, pressure on the region of the appendix, may induce it. This relaxation of the pylorus is in such marked contrast to the resistance which it ordinarily offers to immediate evacuation of the stomach, and occurs so frequently in duodenal ulcer, that numerous theories have been advanced as to

Fig. 84.—The white area indicated by *R* is the six-hour residue in the stomach. Six-hour residue in the duodenum at *D*. Bismuth in small bowel at *A* and *C*.

the mechanism of its production. Unfortunately, this sign is by no means pathognomonic of duodenal ulcer; it is often seen in association with lesions of the gall-bladder, chronic appendicitis, dilated or lax duodeni, neurasthenia, and other conditions, including carcinoma of the stomach. The flow through the gaping carcinomatous pylorus is usually so voluminous and continuous, however, that the experienced observer will rarely confound it with that noted in duodenal ulcer.

A natural sequence of this uninhibited flow is early evacuation of the stomach, and where successive interval examinations are made, the stomach will often be found empty within half or less of the usual time. Some of our cases in which duodenal ulcer was suspected because of the rapid emptying of the stomach were found to be perfectly normal at operation.

Fig. 85.—Same case as in Fig.84, showing the filled stomach. *P*, Deep peristaltic indentations, which were even more marked on the screen; *Pyl.*, pylorus; *D*, residue in duodenum proximal to a stenotic ulcer; *C*, bismuth in small bowel. Operation: Ulcer of the duodenum adherent to the pancreas, producing obstruction.

HYPERTONUS

Various degrees of gastric tone may occur in association with duodenal ulcer. With long-continued duodenal obstruction the stomach may become hypotonic or even atonic, through broken compensation. Such instances, however, are in the minority. More often an orthotonic or hypertonic stomach is found, and we have seen the latter so frequently that we have come to regard it as quite suggestive of duodenal ulcer, especially if the stomach be of the fish-hook form and otherwise normal.

A hypertonic stomach alone is, of course, not necessarily diagnostic, but in general it may be stated that in duodenal ulcer the tendency is toward hypertonicity.

DEFORMITY OF OUTLINE

Irregularities in the outline of the bulbus duodeni, where most ulcers occur, have received considerable exploitation as a reliable indication of duodenal ulcer, chiefly by those radiologists who have depended on plate findings rather than on screen examinations. The technic involves the making of a large number of plates in a given case, and, to establish the diagnosis, every plate must show the same filling defect or deformity at a suspected point, a single plate showing a normal bulb being negative for ulcer. Irregularities of the duodenal wall are by no means pathognomonic of ulcer or even of a duodenal lesion. Distortion by adhesions from a cholecystitis, by pressure, or by incomplete filling is not at all uncommon, and deformity due merely to spasm is rather frequently seen. Further, as is observed in ulcers of the stomach, not all ulcers of the duodenum are sufficiently extensive to produce a local distortion that is radiologically demonstrable. The degree of distention of the bulb and duodenum, and consequently the effectiveness of visualization of their outlines, will depend in part on the ratio between the amount of bismuth flowing through the pylorus and the rate of duodenal evacuation. When the patient stands, the vertical bulbus, which commonly accompanies a fish-hook stomach, will better retain the bismuth by reason of gravity, while the more horizontal bulbus of a steer-horn stomach will drain more rapidly.

As seen at operation, three types of ulcer may be distinguished:

1. Those in which the ulcer is evidently limited to the mucosa and is not seen externally because of the absence of scar tissue. Its presence is determined by the surgeon by palpation, and to a less extent by an area of hyperemia or by petechiæ over the ulcer-bearing area after it has been rubbed with the palpating finger or with gauze.

2. Those with visible scar production but without marked contraction or deformity.

3. Callous ulcers with extensive cicatrization and accompanied *often* by stenosis.

Adhesions are rarely seen in the first type, occasionally in the second, and commonly in the third, especially if there be a perforation or an associated cholecystitis. In the first and second of the above-mentioned types deformity is either absent or so slight

Fig. 86.—*P*, Peristaltic waves, which were stronger at intervals on the screen; *Pyl*, pylorus; *D*, duodenum. No obstruction. Operation showed callous ulcer of duodenum.

as to make its radiologic detection impossible. As a matter of fact, we have seen such ulcers in which no deformity was found either in the Roentgen-ray examination or at operation. In the third type the distortion may be radiologically evident, yet indistinguishable from that consequent on inflammatory lesions extraneous to the duodenum. In this type also stenosis may prevent effective filling of the duodenum with bismuth and thus render negative the diagnosis by this radiologic sign.

LAGGING OF BISMUTH

The normal duodenum empties itself so rapidly that bismuth passing through it is with difficulty visualized on the screen and is rarely seen on the plate unless as an ill-defined, faint shadow. In duodenal ulcer, on the other hand, the bismuth often lags in its progress through the duodenum, and shows distinctly on the screen and plate as a well-outlined shadow. Sometimes the shadow is broken up into separate boluses with vacant areas between, or again it may be more or less continuous. This eccentric progress of the bismuth was one of the first signs noted in the earlier radiologic work; but lagging of the bismuth in the duodenum, even though irregularly distributed, is by no means diagnostic of duodenal ulcer, since it is found quite often where the duodenum is normal and other intra-abdominal lesions exist.

PRESSURE-TENDER POINT

The value of a pressure-tender point over the duodenum as a diagnostic indication of ulcer is rather uncertain. If the contention be true that localized tenderness to pressure of an abdominal viscus exists only when the parietal serosa is involved, then early duodenal ulcers are exempt from this sign. As a matter of fact, tenderness over the duodenal region is quite frequently noted, but whether this tenderness is ascribed to ulcer or to a lesion of the adjacent gall-bladder depends largely on the bias of the observer toward the one or the other. The varying energy of the examiner's manipulation and the differing sensitiveness of patients are also uncertain factors. Yet a decidedly sensitive point, sharply localized to the visualized duodenum, deserves consideration as a contributory sign. Nearly all patients, with or without lesions, have more or less epigastric tenderness in the median line, and this is usually without significance.

SPASMS OF THE STOMACH

A spasmodic hour-glass stomach or slowly traveling incisura may occasionally be seen in cases of duodenal ulcer, but such

spasms occur in association with other lesions and have no specific importance.

One radiologist is on record as stating that he can diagnose duodenal ulcer in 100 per cent. of cases; that it is much easier to diagnose than gastric ulcer, and that he can determine by the Roentgen ray whether or not the ulcer is healed. These claims are not in accord with my experience, nor do they agree with the consensus of opinion of other radiographers. Such extravagant claims do much to bring radiology into disrepute and to prejudice surgeons and clinicians against it. While I believe that the Roentgen ray is perhaps the most valuable adjunct to clinical diagnosis, boastful pretenses and overenthusiasm, which its spectacular accomplishments stimulate, must be suppressed, in order that the skeptics, of whom there are a few, may not deprive their patients of its real benefits, to which they are justly entitled.

STATISTICS

During the ten months covering the period from March, 1913, to January, 1914, inclusive, we have made Roentgen-ray examinations of 2723 persons for lesions of the digestive tract. Of these, 718 later came to operation and 198 were found to have duodenal ulcer.

A radiologic diagnosis of duodenal ulcer was made in 135 of the 198 cases. In 19 a diagnosis was made of obstruction at or near the pylorus, without further attempt at diagnostic refinement. Sixty-eight cases, diagnosed on minor radiologic grounds as duodenal ulcer, were found at operation to have some other lesion, and of these, 29 were gall-bladder affections, 17 chronic appendicitis, and 22 miscellaneous conditions.

Hyperperistalsis of various degrees was noted in 113 (57 per cent.) of the 198 cases of duodenal ulcer. Residue was observed in 72 (36.3 per cent.) of the duodenal ulcer cases. Hyperperistalsis in conjunction with a six-hour residue is worth more than 95 per cent. in diagnosis, and occurred in 49 (24.7 per cent.) of the 198 cases. This combination was seen in 3, or less than 1 per cent., of the 520 cases other than duodenal ulcer.

Six (3.7 per cent.) of 159 cases of lesions of the gall-bladder manifested increased peristalsis. These are the cases which give the greatest difficulty in differentiating them from those of duodenal ulcer.

Hyperperistalsis was shown in 11 (3 per cent.) of the 361 cases of lesions other than duodenal ulcer or gall-bladder.

The exaggerated peristalsis of duodenal ulcer does not appear to be related to the degree of hyperacidity. The average total acidity in 80 cases with hyperperistalsis was 69.7 per cent., while in 72 cases without hyperperistalsis the average total acidity was 74.8 per cent. The highest acidity noted, 120 per cent., occurred in a case with normal peristalsis.

Though the Roentgen ray often fails in the positive diagnosis of duodenal ulcer, its findings have an exclusion value; that is to say, the chance of some other lesion existing is minimized in proportion as the latter is radiologically determinable.

CONCLUSION

Hypermotility, hypertonus, deformity of the cap or bulb, lagging of bismuth in the bulb, pressure-tender point over the duodenum, and spasm of the stomach are minor contributory radiologic signs of duodenal ulcer. The combination of hyperperistalsis and six-hour residue or a diverticulum, when found in an otherwise normal stomach, constitute about the only evidence on which a purely radiologic diagnosis of duodenal ulcer may safely be advanced.

HAIR-BALL IN THE STOMACH: OTHER FOR-
EIGN BODIES IN THE GASTRO-
INTESTINAL TRACT *

WILLIAM C. CARROLL

CASE A107244.—E. C., girl, aged ten. Examined in the
Mayo Clinic June 3, 1914. The child was apparently normal at
birth, and, aside from the contagious diseases incident to child-
hood, had been healthy and strong. She always appeared bright,
and was in the fifth grade at school. The parents noticed no ab-
normal habits until she was about two and one-half years of age,
when she was observed to pull out and chew her hair. It did not
at first occur to the parents that the hair was being swallowed.
The practice was continued even while the child slept, and an at-
tempt was made to overcome it by putting on a tight-fitting night-
cap and mittens. This, however, did no good, as the cap was
pulled off during sleep. When she was about five years of age a
bald spot was noticed on the back of her head. The parents be-
lieve that the habit has greatly diminished during the past five
years, and was scarcely at all noticeable during the past year. Her
appetite had always been good, but of late she had wanted to eat
frequently and only a very little at a time. About ten days before
examination in the clinic she had had a severe headache, with
slight fever and drowsiness. She was moderately constipated.
The abdominal pain, which was absent at the beginning of these
symptoms, began after a few days and became extensive. She
was nauseated and vomited several times. The abdominal pain
became more severe, cramp-like at times, but was not localized.
After remaining in bed one day she felt considerably better.

Examination showed a well-developed girl, mentally bright
and active; scalp covered by thick brown hair; tonsils and ade-
noids very large. The abdomen was large, and especially prom-

inent and tense in the upper right side.   The prominence or mass
moved downward with inspiration.   A distinct tumor, with its
upper end fixed under the left costal arch, could be felt.   The mass,
which was firm and not tender to pressure, filled the epigastrium,
extending to the right just below the costal arch, and filling the
right side of the abdomen (Fig. 87).   The lower portion could

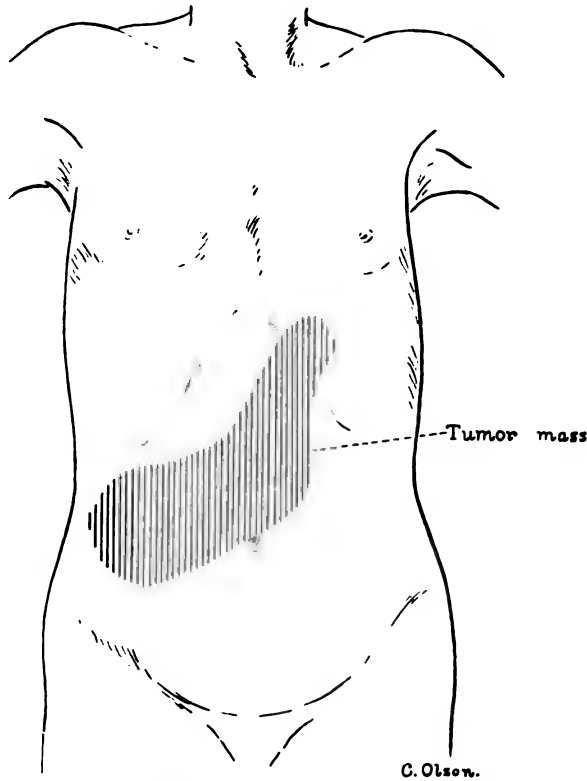Fig. 87.—Diagram showing mass outlined by palpation.

readily be moved in any direction.   The edge of the liver could
be felt independent of the tumor.   There was some doubt as to
the splenic edge, but it apparently was not connected with the
mass.   Neither kidney could be palpated.   There was dullness
over the whole extent of the tumor.   No gastric tympany was
apparent.   Pulse 80; temperature normal.

Urine.—Twenty-four-hour specimen—1050 c.c.; specific gravity, 1012; slight trace of albumin; no casts; no sugar.

Blood.—Hemoglobin, 75 per cent.; erythrocytes, 5,080,000; leukocytes, 7400; polynuclears, 55 per cent.; small lymphocytes, 39.3 per cent.; large lymphocytes, 1.7 per cent.; eosinophiles, 4 per cent. Color index, 0.6.

Diagnosis.—Omental cyst, cystic kidney, sarcoma, and hair-ball of the stomach were considered, but a definite diagnosis was not made, and exploration was done on June 11, 1914, by C. H. Mayo. A median upper abdominal incision was made, and upon opening the peritoneal cavity it was at once seen that the mass was inside the stomach. The incision was enlarged, and the stomach, containing the mass, was brought out on the abdominal wall. The stomach was then opened by a longitudinal incision sufficiently large to extract the mass, which completely filled the gastric cavity and extended for a considerable distance into the duodenum. The incision was closed with chromic catgut and silk, and the abdomen closed without drainage. The patient had an uneventful convalescence and left the hospital on the tenth day.

Pathologic Report.—Hair-tumor weighing two pounds. Dimensions, 12 x 25 x 7 cm. (Fig. 88).

Hair-ball in the stomach is comparatively rare in man. Butterworth[1] (1909) collected 41 cases from the literature and reported one of his own. Moore[2] (1914) reviewed 54 cases. Of the latter, 48 were in women and 5 in men. The majority were mentally sound. The duration of the habit of chewing and swallowing hair varied from two to twenty-two years. He found that there was a mortality of 86 per cent. in those not operated on. Twenty-eight patients have been operated on, with two deaths—a mortality of 7 per cent. In 4 cases the results of treatment were not given.

Only a very small percentage of these cases was diagnosed definitely. Among the diagnoses given were enlarged liver or spleen, omental cyst, pancreatic cyst, cystic kidney, and malignancy. one patient vomited small portions of hair, while another passed small masses of hair through the bowels.

Holland[3] first called attention to the value of the x-ray in the diagnosis of hair-ball in the stomach, showing how accurately the

shadow takes the usual J-shaped appearance. When the hair-
ball is large, a picture taken immediately after a small portion of

Fig. 88.—Posterior view of hair-ball tumor: gross specimen.

the barium is swallowed shows a cap-like formation at the cardia.
This is due to the barium being blocked by the tumor. After
giving more barium and waiting a short time, a picture will show

the whole stomach mapped out by the barium lying between the tumor and the wall of the stomach.

Medical literature contains many striking examples of foreign bodies in the stomach, not only in man, but also in animals, and perhaps more frequently in the latter. Many solid or fluid substances which play a rôle in our general economy may, under abnormal conditions, act as foreign bodies. The age, sex, occupation, and mental condition of the patient are in many instances predisposing etiologic factors. Every museum contains specimens demonstrating the variety of foreign bodies that may be taken into the stomach and lodge there. In general, these bodies may be divided into two classes: (1) Hard objects, as nails, screws, knives, spoons, forks, buttons, coins, glass, bones, seeds, etc. (2) Soft objects, as hair, strings, vegetable fibers, etc.

Vandivert and Mills[4] report a case of a woman thirty-three years of age who had suffered from acute mania. At postmortem 1446 articles were found. The list included 453 three to 20-penny nails, 42 screws $\frac{1}{2}$ to $2\frac{1}{2}$ inches in length, 9 bolts, and numerous other articles, such as teaspoon handles, nail-files, thimbles, button, tacks, pins, needles, etc. One needle was found in the esophagus and another penetrating the base of the left lung.

Warren and Gould[5] cite two interesting cases of foreign bodies in the stomach. In the first case were found nails, screws, knife-blades, and various other articles, numbering in all 127, and weighing one pound. In the second were found nails, buttons, and glass weighing two pounds.

DaCosta[6] states that the lodgment of a foreign substance in the stomach is accidental.

In general, the dangers to be feared from foreign bodies are obstruction and perforation, the latter being the more frequent. Perforation may take place soon after the ingestion of the object, or it may be delayed, depending upon the size and shape of the body and the location in which it becomes lodged. However, it is of comparatively rare occurrence, considering the number of foreign substances which traverse the alimentary canal. Perforation is usually slow and permits adhesions to surround the

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area, thus protecting the general abdominal cavity from infection. Localized abscesses may form and open to the exterior or into a viscus.

Foreign bodies in animals are due to their propensity to lick and swallow various objects. Cattle chew their food very little before swallowing, and are, therefore, liable to ingest objects mixed with their food. Hair and indigestible vegetable fibers, as from ripe field clover, etc., often form round or oval bodies which are covered by a deposit of mucus and salts. These bodies may vary in size, and remain in the fore-stomach of cattle for a long period. They are often found postmortem in horses, cows, sheep, and Angora cats.

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PAPILLOMA OF THE GALL-BLADDER *
Report of 85 Cases

HAMNER CARSON IRWIN AND WILLIAM CARPENTER MAC-
CARTY

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Papillomas of the gall-bladder have been seen so frequently in
the experience of the writers and have received so little attention in
literature that it seems advisable at this time to record and describe
the conditions somewhat in detail, especially since they belong
to the neoplasms, a group which, as our knowledge increases, is
becoming more intimately associated with chronic inflammatory
reaction.

In 1909 one of us (MacCarty †) included and classified the
condition, reporting one case in a series of 365 gall-bladders which
had been removed at operation. It was described as a part or a
stage of a reaction of the tissues of the gall-bladder to one or more
irritants.

In the series of 365 gall-bladders, the lesions grouped themselves
in the following manner:

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Cholecystitis catarrhalis carcinomatosa.

Cholecystitis chronica.

Cholecystitis chronica cystica.

Cholecystitis purulenta necrotica.

Pericholecystitis acuta and chronica.

inent and tense in the upper right side. The prominence or mass moved downward with inspiration. A distinct tumor, with its upper end fixed under the left costal arch, could be felt. The mass, which was firm and not tender to pressure, filled the epigastrium, extending to the right just below the costal arch, and filling the right side of the abdomen (Fig. 87). The lower portion could
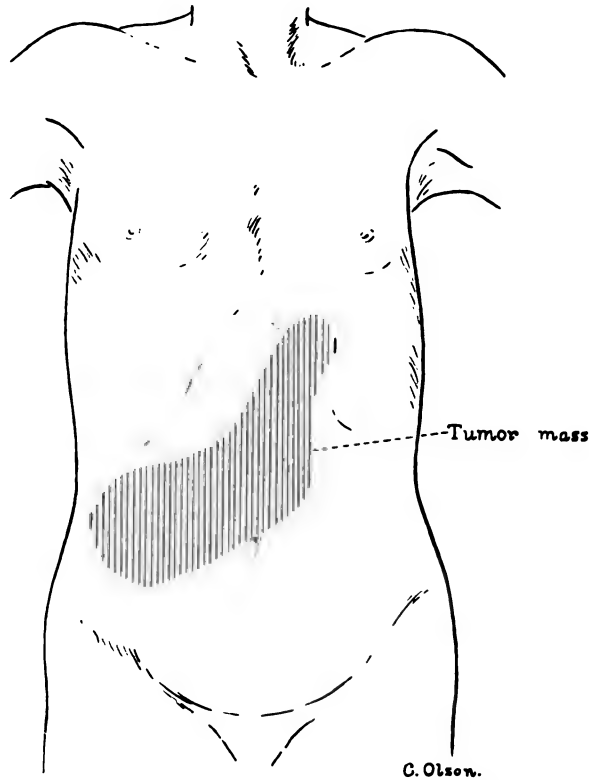

C. Olson.

Fig. 87.—Diagram showing mass outlined by palpation.

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Urine.—Twenty-four-hour specimen—1050 c.c.; specific gravity, 1012; slight trace of albumin; no casts; no sugar.

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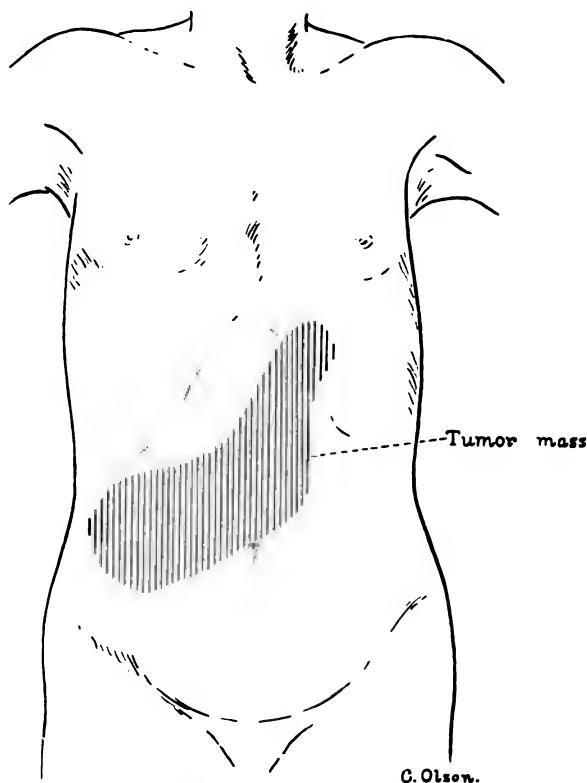

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Diagnosis.—Omental cyst, cystic kidney, sarcoma, and hair-ball of the stomach were considered, but a definite diagnosis was not made, and exploration was done on June 11, 1914, by C. H. Mayo.   A median upper abdominal incision was made, and upon opening the peritoneal cavity it was at once seen that the mass was inside the stomach.   The incision was enlarged, and the stomach, containing the mass, was brought out on the abdominal wall. The stomach was then opened by a longitudinal incision sufficiently large to extract the mass, which completely filled the gastric cavity and extended for a considerable distance into the duodenum.   The incision was closed with chromic catgut and silk, and the abdomen closed without drainage.   The patient had an uneventful convalescence and left the hospital on the tenth day.

Pathologic Report.—Hair-tumor weighing two pounds.   Dimensions, 12 x 25 x 7 cm. (Fig. 88).

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Only a very small percentage of these cases was diagnosed definitely.   Among the diagnoses given were enlarged liver or spleen, omental cyst, pancreatic cyst, cystic kidney, and malignancy. one patient vomited small portions of hair, while another passed small masses of hair through the bowels.

Holland[3] first called attention to the value of the *x*-ray in the diagnosis of hair-ball in the stomach, showing how accurately the

shadow takes the usual J-shaped appearance. When the hair-ball is large, a picture taken immediately after a small portion of

Fig. 88.—Posterior view of hair-ball tumor: gross specimen.

the barium is swallowed shows a cap-like formation at the cardia. This is due to the barium being blocked by the tumor. After giving more barium and waiting a short time, a picture will show

the whole stomach mapped out by the barium lying between the tumor and the wall of the stomach.

Medical literature contains many striking examples of foreign bodies in the stomach, not only in man, but also in animals, and perhaps more frequently in the latter. Many solid or fluid substances which play a rôle in our general economy may, under abnormal conditions, act as foreign bodies. The age, sex, occupation, and mental condition of the patient are in many instances predisposing etiologic factors. Every museum contains specimens demonstrating the variety of foreign bodies that may be taken into the stomach and lodge there. In general, these bodies may be divided into two classes: (1) Hard objects, as nails, screws, knives, spoons, forks, buttons, coins, glass, bones, seeds, etc. (2) Soft objects, as hair, strings, vegetable fibers, etc.

Vandivert and Mills[4] report a case of a woman thirty-three years of age who had suffered from acute mania. At postmortem 1446 articles were found. The list included 453 three to 20-penny nails, 42 screws $\frac{1}{2}$ to $2\frac{1}{2}$ inches in length, 9 bolts, and numerous other articles, such as teaspoon handles, nail-files, thimbles, button, tacks, pins, needles, etc. One needle was found in the esophagus and another penetrating the base of the left lung.

Warren and Gould[5] cite two interesting cases of foreign bodies in the stomach. In the first case were found nails, screws, knife-blades, and various other articles, numbering in all 127, and weighing one pound. In the second were found nails, buttons, and glass weighing two pounds.

DaCosta[6] states that the lodgment of a foreign substance in the stomach is accidental.

In general, the dangers to be feared from foreign bodies are obstruction and perforation, the latter being the more frequent. Perforation may take place soon after the ingestion of the object, or it may be delayed, depending upon the size and shape of the body and the location in which it becomes lodged. However, it is of comparatively rare occurrence, considering the number of foreign substances which traverse the alimentary canal. Perforation is usually slow and permits adhesions to surround the

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area, thus protecting the general abdominal cavity from infection. Localized abscesses may form and open to the exterior or into a viscus.

Foreign bodies in animals are due to their propensity to lick and swallow various objects. Cattle chew their food very little before swallowing, and are, therefore, liable to ingest objects mixed with their food. Hair and indigestible vegetable fibers, as from ripe field clover, etc., often form round or oval bodies which are covered by a deposit of mucus and salts. These bodies may vary in size, and remain in the fore-stomach of cattle for a long period. They are often found postmortem in horses, cows, sheep, and Angora cats.

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PAPILLOMA OF THE GALL-BLADDER *
Report of 85 Cases

HAMNER CARSON IRWIN AND WILLIAM CARPENTER MAC-
CARTY

Papillomas of the gall-bladder have been seen so frequently in
the experience of the writers and have received so little attention in
literature that it seems advisable at this time to record and describe
the conditions somewhat in detail, especially since they belong
to the neoplasms, a group which, as our knowledge increases, is
becoming more intimately associated with chronic inflammatory
reaction.

In 1909 one of us (MacCarty †) included and classified the
condition, reporting one case in a series of 365 gall-bladders which
had been removed at operation.   It was described as a part or a
stage of a reaction of the tissues of the gall-bladder to one or more
irritants.

In the series of 365 gall-bladders, the lesions grouped themselves
in the following manner:

Cholecystitis catarrhalis acuta.
Cholecystitis catarrhalis chronica.
Cholecystitis catarrhalis papillomatosa.
Cholecystitis papillomatosa malignum.
Cholecystitis catarrhalis carcinomatosa.
Cholecystitis chronica.
Cholecystitis chronica cystica.
Cholecystitis purulenta necrotica.
Pericholecystitis acuta and chronica.

inent and tense in the upper right side. The prominence or mass
moved downward with inspiration. A distinct tumor, with its
upper end fixed under the left costal arch, could be felt. The mass,
which was firm and not tender to pressure, filled the epigastrium,
extending to the right just below the costal arch, and filling the
right side of the abdomen (Fig. 87). The lower portion could

Fig. 87.—Diagram showing mass outlined by palpation.

readily be moved in any direction. The edge of the liver could
be felt independent of the tumor. There was some doubt as to
the splenic edge, but it apparently was not connected with the
mass. Neither kidney could be palpated. There was dullness
over the whole extent of the tumor. No gastric tympany was
apparent. Pulse 80; temperature normal.

Urine.—Twenty-four-hour specimen—1050 c.c.; specific gravity, 1012; slight trace of albumin; no casts; no sugar.

Blood.—Hemoglobin, 75 per cent.; erythrocytes, 5,080,000; leukocytes, 7400; polynuclears, 55 per cent.; small lymphocytes, 39.3 per cent.; large lymphocytes, 1.7 per cent.; eosinophiles, 4 per cent. Color index, 0.6.

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Cholecystitis chronica.

Cholecystitis chronica cystica.

Cholecystitis purulenta necrotica.

Pericholecystitis acuta and chronica.

Since the original report was made, more gall-bladders have been removed in earlier stages of inflammatory reaction, and this
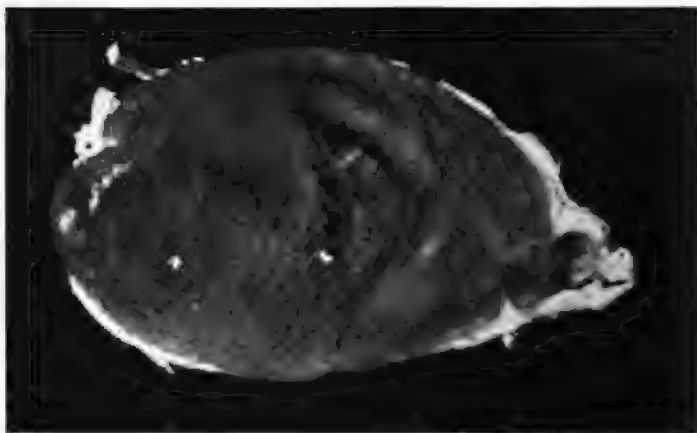
Fig. 89.

Figs. 89, 90, 91, and 92.—(A97358, A65036, and A78954.) Show gall-bladders which contain various size papillomas in different positions ranging from the fundus to the neck.
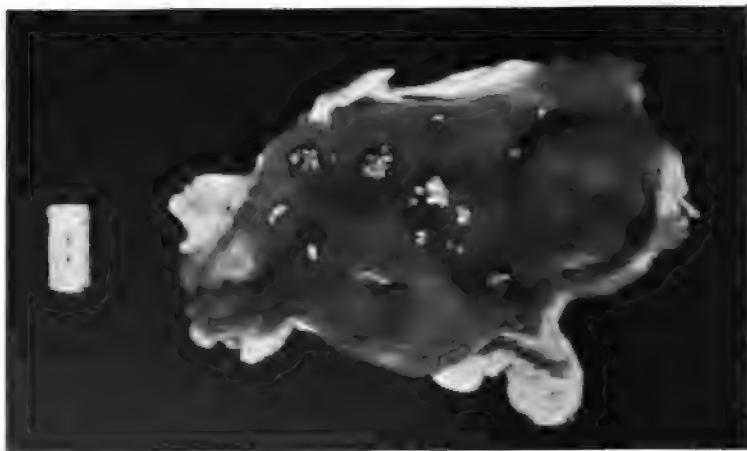
Fig. 90.

fact is, probably, responsible for the frequency of the papillomatous condition which has been recently found.

Of 2168 gall-bladders which have been examined between January 1, 1907, and January 1, 1915, 85 specimens have been found in which one or more papillomas have been seen (Figs. 89–95).

In all cases the mucosa was intact. The papillomas vary

Fig. 91.
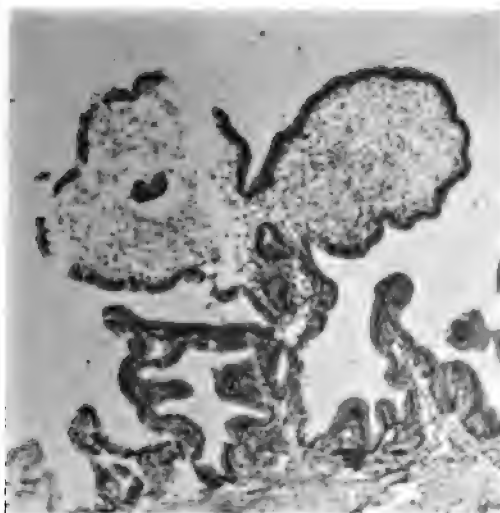
Fig. 92.

Fig. 93.

Figs. 93 and 94.—(A99469 and A96563.)   Low-power sections showing the papillomatous outgrowths from the mucosa.
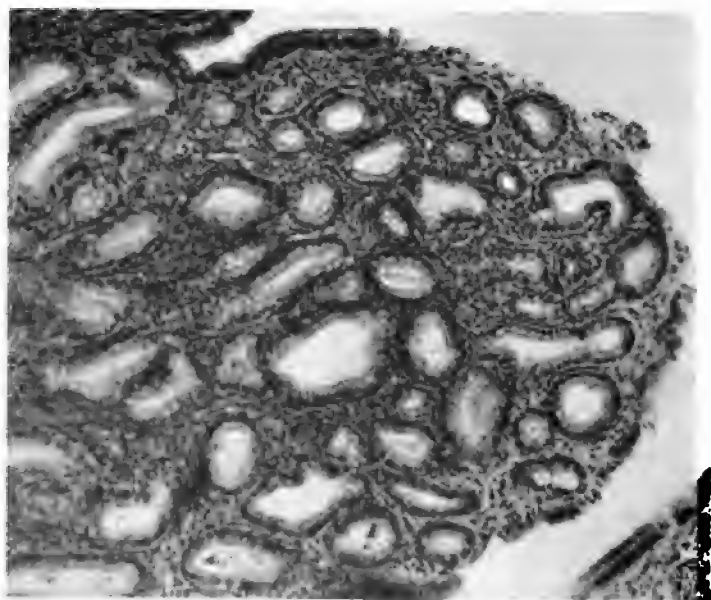
Fig. 94.
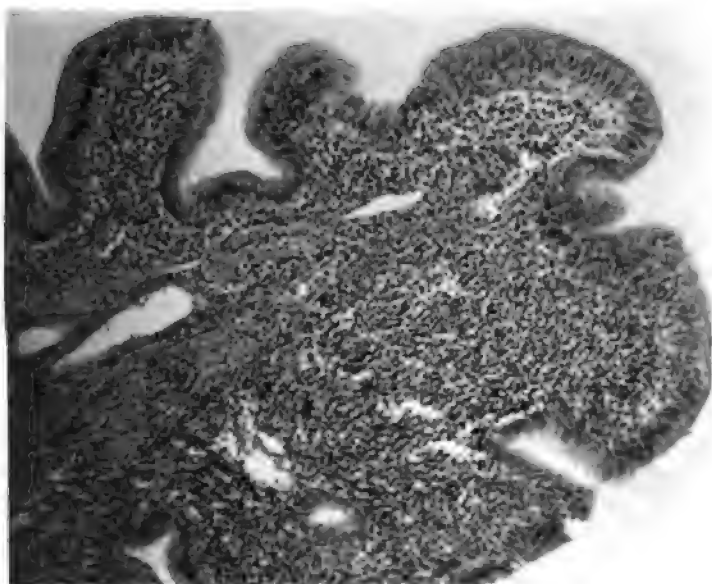
Fig. 95.
Figs. 95, 96, 97, and 98.—(A98808, A96563, A78954, A99469, and A78954.) Present higher magnifications of the epithelium and stroma.
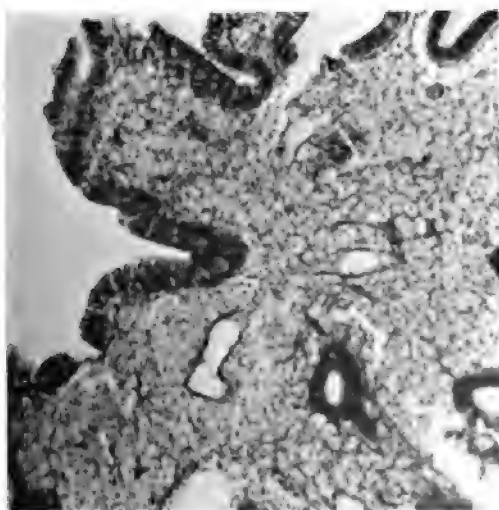
Fig 96.

Fig. 97.
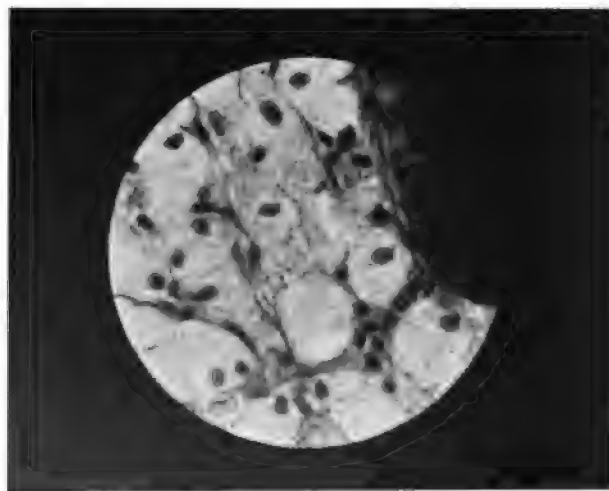
Fig. 98.

from twice to five or six times the length of normal villi. They are usually pedunculated, frequently racemose, and usually white or yellow. They appear in any portion of the organ, being con-fined neither to the neck nor to the fundus.

Upon microscopic section they appear to be hypertrophic villi, the tissue elements of which present a hyperplastic condition. The connective tissue and glandular tissues are greatly increased, the latter being so distorted that sections cut the glands in many different planes. The epithelium of the glands is hypertrophic and occasionally hyperplastic, and practically always completely covers the growth.

In the stroma one often finds large round or oval cells which contain fat or some fatty substance, this condition probably being responsible for the yellowish, gross appearance of the growths (Figs. 96–98).

In no case were there any signs of early carcinoma, although similar hypertrophic conditions of the villi have been seen in association with carcinomatous outgrowths of the gall-bladder.

The condition occurred in cholecystitis catarrhalis acuta, cholecystitis catarrhalis chronica, cholecystitis catarrhalis cystica, cholecystitis catarrhalis carcinomatosa, and cholecystitis catarrhalis purulenta necrotica. It occurred with and without the association of stones, and was more frequent in females than males, probably due to the fact that more gall-bladders were removed in females.

The writers take the liberty of reporting these cases in order to stimulate observers to watch for the association of the condition with malignant changes in the mucosa, since it is associated with chronic inflammation and has been associated with late carcinoma.

It is quite possible, in the light of recently discovered facts relative to the stages of epithelial hyperplasia from chronic irritation, that these fibro-epithelial proliferations might also present the stages which are apparently a part of a cytologic reaction which sometimes ends in a malignant condition.

RESECTION OF THE FIRST PORTION OF THE LARGE INTESTINE AND THE RESULTING EFFECT ON ITS FUNCTION *

WILLIAM J. MAYO

Human beings vary in their internal anatomy in about the same degree that they vary in their external form and configuration. Were a man who was thin and 6 feet high to ask us to make him fat and 5 feet 6 inches high by operating on him, we would think him mentally deranged. Yet how frequently in the past have we attempted to correct surgically the internal anatomy because of variations from the average normal, especially the position of the abdominal viscera?

It is less than ten years since nephrorrhaphy, ventrofixation, gastrorrhaphy, and kindred operations were resorted to on indications which would not be accepted to-day. We have come to appreciate the fact that comparatively few of the abdominal viscera have unchangeable anatomic characteristics, and that variations within limits are not to be considered abnormal.

The large intestine, with its short heredity and changing function, has no such fixed characteristics as has the more primitive small intestine. Arising on the left side of the body, the head of the colon swings to the right, but does not reach its normal habitation until after birth. The peritoneal cavity has then already been formed, and its attachments on the right side may take on the character of adhesions, in many instances causing that condition which Jackson[1] has so aptly termed a "veil." This loose-

ness of attachment of the ascending colon and hepatic flexure permits of freer movement of the right kidney. The terminal ileum normally comes up out of the pelvis and enters the cecum at an acute angle. The ileocecal valve is a sphincter mechanism acting to hold the ileal contents and delay their progress, and this stasis within limits is normal. Early in fetal life the ileum becomes attached to the inner side of the cecum. This fixation prevents expansion on the inner side and, because of its inability to expand in all directions, the cecum assumes a lop-sided appearance. An exaggeration of the sustaining bands is often called ileal kinks.

The large intestine, within normal limits, varies in length and position, especially the transverse colon and sigmoid. The high fixation of the splenic flexure of the colon, economically taking the place of a muscular sphincter, is a fixed characteristic and performs an important function. It holds within the proximal half of the large intestine the ingesta which have been passed into it from the small intestine and delays their progress that fluids and nutritive material may be absorbed therefrom. When the waste remnants move beyond the splenic angle, they pass rapidly through the descending colon, which acts as the vestibule to the sigmoid, the normal fecal container. As pointed out by Rokitansky,[2] more than sixty years ago, the descending colon is normally empty.

Usually when we speak of the cecum we mean the cecocolon or head of the colon, which includes the cecum, ascending colon, and hepatic flexure. The cecum itself is the end-pouch only, and is but from $1\frac{1}{2}$ to 3 inches in length.

It is altogether probable that in the past too much importance has been attributed to purely incidental changes in the position and attachments of the large intestine. Bands, kinks, and adhesions of a normal character have been given a fictitious rôle in the supposed production of symptoms which were not in themselves mechanical. Adhesions, bands, and kinks are not usually congenital in the sense that they are formed prenatally and then remain as formed, but they change in character throughout life.

The interesting work of Lane,[3] Pilcher,[4] Gerster,[5] Gray,[6] Pringle,[7] Binnie,[8] Jackson,[1] Eastman,[9] Flint,[10] and many others has thrown much light on the origin of these bands. We are indebted to the pioneer work of Lane for calling our attention to the fact that in the large intestine may lie the cause of much human misery. While I do not agree with Lane in the great stress which he lays on the rôle of bands, kinks, etc., I am convinced that he has discovered a great physiologic truth not heretofore recognized, and he must be fully credited with bringing forward this most important question. Whether or not we agree with him, we must at least recognize the facts on which his contention rests.

The villi of the small intestine are to man as roots to a tree. In early fetal life the first half of the large intestine contains villi the same as the small intestine; and while these villi in later development are lost as anatomic structures, the power of absorption remains. We speak of rectal feeding as though food were actually absorbed in the rectum. As a matter of fact, food or other material placed in the rectum is promptly carried by reverse peristalsis toward the head of the colon for absorption and assimilation.

What is the function of the large intestine? Beyond the splenic flexure it is to a great extent a storage organ. But proximal to the splenic flexure the colon, and especially the cecocolon, has a most important assimilative function. We know that in the carnivora the large intestine is small as compared with its great size and importance in the herbivora. In the herbivora the large intestine, and especially the cecocolon, may be compared to a silo in which fermentation of vegetable matter takes place, freeing nutritive material of the greatest value.

The function of the appendix, a part of the large intestine, is practically unknown. The organ in man has been looked on as the vestigial remnant of a herbivorous cecum. Keith[11] dissents from this view, believing that the appendix is a lymphoid organ having a function comparable to that of the tonsil and solitary follicles of the intestine. Ribbert[12] has demonstrated that beginning at adolescence a progressive involution takes place in the

appendix, and that in persons at the age of fifty one-half of all appendices show age characteristics.   An appendix which would

Fig. 99.—Anatomy of the lower ileum and first half of the large intestine.

be normal in a person at fifty years would be abnormal in a child. The same may be said of the tonsil.

C. H. Mayo,[13] in 1903, pointed out the surgical significance of the progressive atrophy of the lymphoid structures of the body after adolescence, thus explaining why cancer in old persons does not spread with the rapidity it does in youth, because of the atrophy of the lymphatics.

We must therefore look on the appendix as a lymphoid organ which in early life has some value in connection with cecocolic metabolism. It is interesting to note that in the carnivora, which do not have an appendix, lymphoid tissue of the same nature as that found in the appendix is to be found at the apex of the cecum, the site of the appendix were it present.[14]

It has been suggested that the appendix may, through chronic inflammation, vaccinate the patient against subsequent colon infections.

Reasoning from analogy, we can say that the functional activity of the proximal half of the large intestine concerns vegetable intake. It has been shown that within one hundred years the flesh intake of man has increased four times.[15] The decomposition of unassimilated flesh food develops poisonous substances. It is reasonable to suppose that when these end-products are passed into the large intestine, which has developed to a full extent only the power of caring for vegetable material and fluids, such products may be absorbed, thus disturbing the sympathetic balance and producing many of the symptoms which we speak of in our ignorance as neurasthenia, and which sometimes have been thought to be the result of mechanical conditions, bands, kinks, etc. In this connection a peculiar type of constipation with a thin-walled bowel with no abdominal distention may frequently be noted. The abdomen is soft and silent, as compared with that encountered in true mechanical obstruction, with its intestinal stiffening, colic, and abdominal distention. The general condition of the patient often well illustrates this sympathetic disturbance. A severe case may even resemble an exophthalmic goiter, for which it may be mistaken. Why may not these persons be cured by a
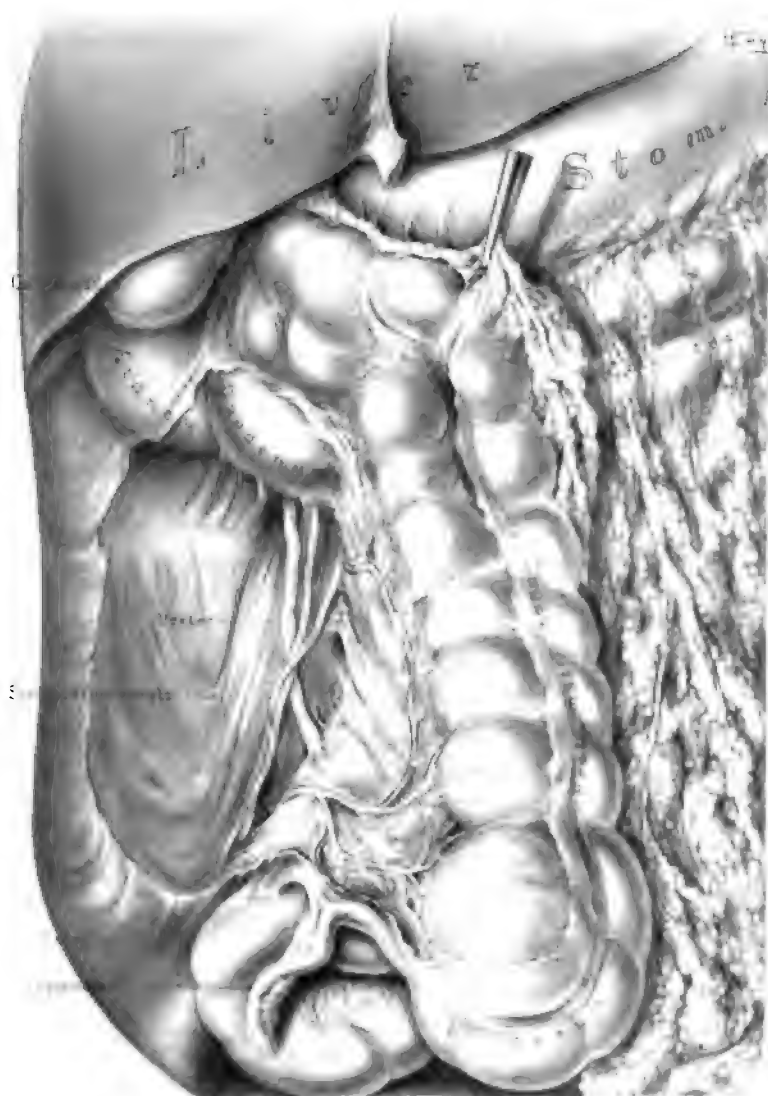
Fig. 100.—Division of the peritoneum, which binds cecum and ascending colon to the abdominal
wall. Retroduodenum, spermatic vessels, and ureter exposed.

purely vegetable diet? When we consider that man as a species is at least five hundred thousand years old, and that his present characteristics have slowly evolved,—so slowly, indeed, that the evidences of prehistoric man show him anatomically to be essentially the same as to-day,—the futility of attempting to change during the lifetime of a single individual the whole history of race metabolism is evident.

Adami[16] objects emphatically to the use of the term "autointoxication," since proof of such process is lacking. He believes that a low grade of bacteriemia with a local *subinfection* of various vital organs is responsible for the disturbance, and in this he is probably correct in most cases; but obstruction of the bowels produced experimentally by Whipple, Stone, and Bernheim[17] shows the poisonous effect of the secretions of the upper jejunum and duodenum when acutely blocked, independent apparently of infection, an effect which these authors speak of as an "intoxication." Clinical experience in acute intestinal obstruction as it occurs in man seems to bear out these experiments. For this reason a high enterostomy in acute intestinal obstruction gives quicker and surer relief than one down closer to the actual point of obstruction (McKenna[18]). Vaughan,[19] in his notable work on protein metabolism, shows the specific character of the poisonous effects which are produced by failure properly to split up proteins and their relation to food idiosyncrasies and anaphylaxis.

Hypersecretion or hyposecretion of the thyroid and hypophysis and the various other glands of internal secretion may have its counterpart in like conditions of the glands of the intestinal mucosa. In lieu of a more expressive term, and in the absence of a scientific explanation of the clinical phenomena, intoxication may be used temporarily as a term to express the hypothetic condition. Intoxication is at least a graphic term for these conditions, meaning the absorption of chemical substances, no matter how produced—substances which may be absorbed without leaving in their path infective lesions in the mucosa of the intestine at the place of absorption or resulting in the bacterial invasion of organs.

Putting aside for the moment these anatomic and physiologic

Fig. 101.—Results after removal of 10 inches of ileum, appendix, cecum, ascending colon, hepatic flexure, and one-fourth of transverse colon.   End-to-side ileocolostomy.   Running suture closing peritoneum of posterior wall.

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considerations, I wish to discuss the effect of the removal of the cecocolon, first as a means of physiologically limiting absorption, and, second, as to its effect on the storage function of the bowel, that is, on constipation. These two conditions go hand in hand: namely, so-called stasis of the large intestine with a train of nervous derangements and constipation. In 1900 I reported[20] some cases of obstinate constipation which had been cured by an enlargement of the ileocecal orifice, and suggested that constipation may be many times primarily dependent on constipation of the small bowel; that food products might be retained in the small intestine for too great a length of time and not furnish the necessary chemical stimulation to activate the large intestine. I am convinced that the observations which were made at that time and which have been continued in the intervening years were essentially true, and that we may go still further and say that retention of these products, not only in the small intestine, but in the cecocolon, has a similar effect in diminishing the stimulation to action in the storage half of the large intestine. Lane,[21] by means of ileocolostomy, has apparently demonstrated the value of this stimulation and its effect not only on constipation, but also on the metabolism of the individual. Hertz and Newton[22] have shown that food intake furnishes a gastro-iliac reflex, and the ileocecal valve opens and allows the lower ileum to empty its contents. A gastrocolic reflex occurs simultaneously, and the cecocolon forces its contents onward. It is possible that the ileocecal valve is controlled by the cecocolon, just as the pylorus is controlled by the duodenum. Ileocolostomy, however, in a certain percentage of cases, especially in adults, leads to an impaction in the disused colon through reversed peristalsis, and thus in some cases to a continuous absorption of poisonous products quite as though ileocolostomy had not been performed.

From a small number of patients—about 20—in whom exaggerated conditions of cecocolic stasis and the train of general nervous symptoms which go with it, and in all of whom constipation amounting to obstipation was present, we have removed 10 inches of the terminal ileum, appendix, cecum, ascending colon,

hepatic flexure, and a portion of the transverse colon, but not trespassing to a great extent on the part of the transverse colon which contains the omentum. If all the omentum is removed, as happens in colectomies, in many cases intestinal adhesions of the most severe type subsequently occur, often causing unfortunate sequelæ. The cases in which operation was performed were all an advanced grade, and in all there were bands, kinks, adhesions, and possibly obstruction, but if so, of the peculiar silent type with a soft abdomen and without muscular hypertrophy of the intestinal wall.

In the cases in which we have made the above-mentioned resection and joined the end of the ileum to the side of the transverse colon, there has usually been a marked improvement in the general condition of the patients, and in 87 per cent. relief from the constipation. In nearly all these patients the appendix had previously been removed, and in a number of them other operations, such as elevation and fixation of the cecum, combined with narrowing of its lumen, etc., had been done without relief. To test the question of the effect of eliminating the ileocecal mechanism and removing the proximal colon in constipation we have grouped together all the cases in which the head of the colon was removed without regard to the pathologic conditions which lead to the operation, and have investigated the effect the operation has had on the evacuation of the large intestine. It was found that nearly all the patients who had been constipated before the operation have been much relieved postoperatively. Yet in but one case has diarrhea been manifested. It would seem a reasonable assumption, therefore, that in physiologic disturbance of the terminal ileum and cecocolon lies the cause, in some cases at least, of the protean manifestations of intestinal toxemia and constipation, and that the removal of the cecocolon will relieve many of these patients.

Although the operation is a serious one, we have lost no patients operated on for this condition. The number of persons whose condition in our opinion would warrant the risk, however, is comparatively small, and I cannot but deplore the wide-spread adop-

tion by the medical profession of surgical measures for this or allied conditions while it is in the experimental stage, with little evidence to show that the supposed cures are permanent. When one looks back over the fads and fancies in medicine, especially as applied to the so-called neurasthenic group of patients, one may well pause and make haste slowly.

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INTESTINAL POLYPOSIS *

WILLIAM C. CARROLL

Intestinal polyposis is a comparatively rare disease, occurring especially in the young and middle aged. Its etiology is uncertain. Polypoid growths may occur at any point along the gastro-intestinal tract, but in the majority of cases they are found in the large intestine, usually at its turning-points, and in the rectum. The size of the growths varies from a mere beginning up to the size of an orange. Occasionally they have been found at autopsy in persons dying from other conditions. Apparently these growths had not produced symptoms.

The following is a report of a case recently examined in the Mayo Clinic:

CASE A114349.—H. A. S. Male, aged thirty-eight, married. Examined September 2, 1914. One brother has tuberculosis, otherwise the family history is negative. The patient denies venereal diseases, but admits having indulged in alcoholics quite freely at times. He has had several attacks of malaria, but has otherwise always been well and strong, up to three months prior to examination. The first symptoms noted were loss of weight and general malaise. At the onset he had also several spells of nausea and vomiting and some epigastric distress. During the last six weeks have occurred four attacks of sharp pain around navel and across upper abdomen, later becoming localized in the right iliac fossa. Nausea and vomiting accompanied each of these attacks, the most severe of which occurred three weeks before he came to the clinic. At that time nourishment had not been retained for three days. The attacks came on at about ten-day intervals, the last one a week previous, at which time he had a

chill, accompanied by a temperature of 102.5° F., but no pain.
Some degree of soreness had persisted in the right iliac fossa, and
a few days following the last attack a mass could be palpated and
easily outlined in the right lower abdomen. Appetite good;
bowels regular; loss in weight during last ten months, 40 pounds.
Systolic blood-pressure, 120 mm.; diastolic, 85 mm. Pulse, 100.
Temperature, 98.8° F. Urine: Specific gravity, 1028; acid, no
albumin, sugar, nor casts. Leukocyte count, 11,200.

In view of the history and physical findings a diagnosis of an
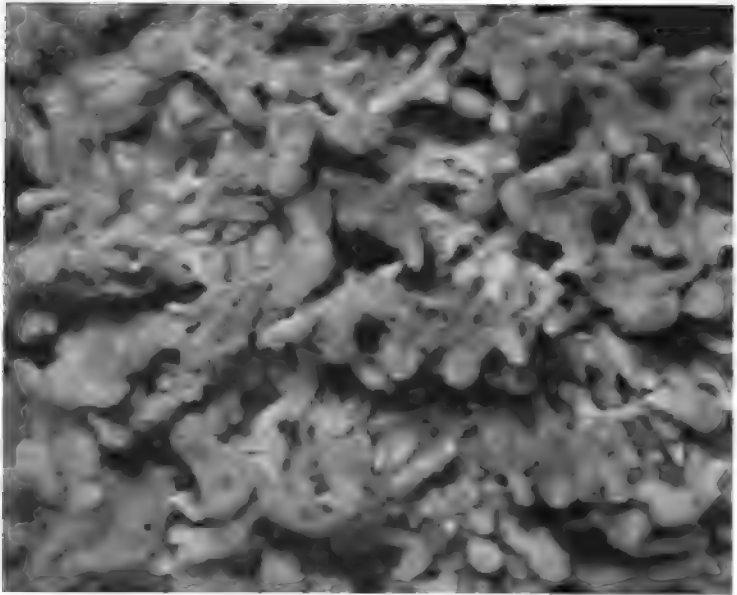
Fig. 102.—Marked polypoid growth, approximately actual size.

inflammatory tumor of the right lower abdomen was made and
operation advised and accepted.

Operation.—On September 4 1914. The operation was per-
formed by E. S. Judd. A right rectus incision was made and the
abdomen opened. The general exploration was negative except
for the cecum, ascending colon, and a portion of the transverse
colon, which were thickened and firmer than normal. By grasping
this portion of the bowel and passing it between the fingers the inner
surface appeared to be covered with a papillary growth, and a

diagnosis of papillary colitis or polyposis was made. A resection was done of the affected portion, which included 6 inches of the ileum, cecum, ascending colon, and a portion of the transverse. An end-to-side anastomosis between the ileum and transverse colon was then made, and the abdominal wound closed without drainage. The patient left the hospital on the fourteenth day and made an uneventful recovery.

Pathology.—The gross appearance of the specimen is shown in Fig. 102. The entire mucous membrane is covered with growths,
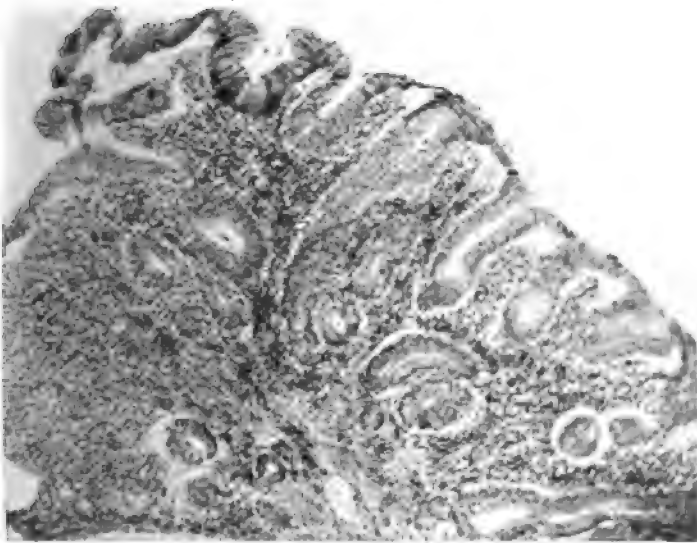
Fig. 103.—Section of a polypus showing the normal mucous membrane, increase in the glands, and lymphatic infiltration.

some of which form small, rounded elevations, others on long pedicles which vary in length and size, while in many places branched filaments are to be found.

Microscopically the mucous membrane consists of one layer of columnar epithelium similar to that which lines the normal intestine. There is a marked increase in the glands, which are long, tortuous, and branched. These glands are lined with columnar epithelium, among which are a great many goblet cells. In certain areas retained secretion, clinging to the surface of the cells,

may be seen. Blood-vessels show some congestion, and the whole thickness of the specimen shows a distinct infiltration of lymphocytes (Figs. 103-105).

Some observers have noted a peculiar family tendency in these cases. Doering[1] states that Zahlman records an instance in which six brothers and sisters died of the disease.

Gastric polypi are similar in structure to those found in the
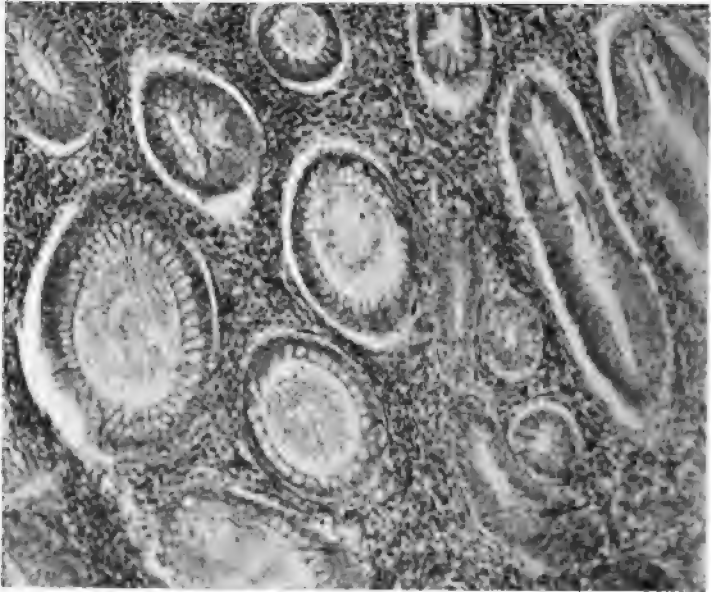
Fig. 104.—Higher power section, showing glands containing many goblet-cells.

intestine. They are usually found along the greater curvature, near the pylorus. They may be adenoma, fibroma, myoma, or lipoma. Wade[2] describes a case of intussusception of the stomach and duodenum caused by the presence of a benign pedunculated fibroma. Gibson[3] cites a case of pedunculated polypus just inside the pylorus which caused intermittent obstruction—a ball-valve action.

Intestinal polypi may be single or multiple, the latter being

more common.   Rectal polypi are not uncommon, and, according
to Cripps,[4] two common forms of polypi are to be found in the
rectum: the fibrous type, which is a pedunculated tumor and com-
posed for the most part of fibrocellular tissues, and the other the
adenoid polypi, which are extremely vascular and consist of gland
tissue.   These are usually single.   Extremely rare conditions
are the dermoid and the cystic polypi.   Doering[1] states that there
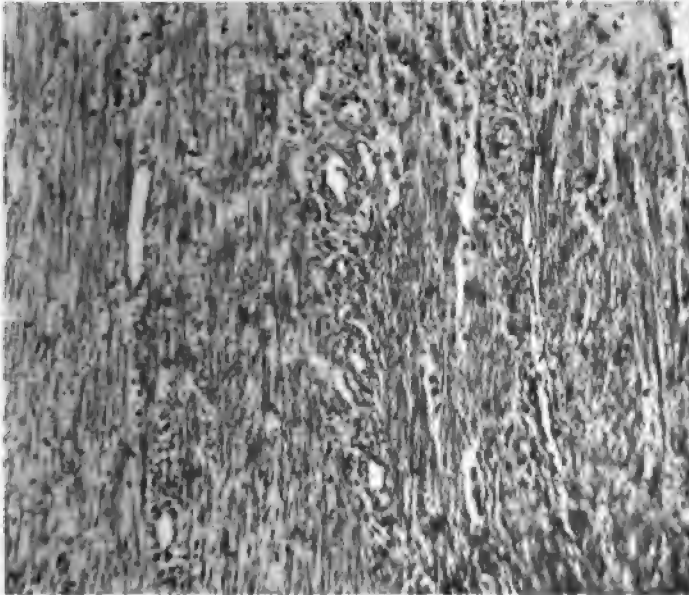
Fig. 105.—Section through the muscular coat, showing the marked lymphocytic infiltration.

is a greater tendency to malignant degeneration in the rectum, and
cites 24 cases of rectal polyposis in which carcinoma was present
in 15.

Occasionally cases have been seen at the Mayo Clinic which,
on proctoscopic examination, showed several polypi high up in the
rectum.   They were cauterized with the high frequency current.
Microscopically they were of the adenomatous type.   Another
class of cases which have shown rectal polypi have been those of

intestinal infection. These were also treated with the high frequency. In a few instances small carcinomatous polypi high up in the rectum, two to four in number, have been the means of making a diagnosis of a malignant growth higher up than could be reached with the proctoscope. These diagnoses have been verified by abdominal exploration.

The growths often cause obstruction and intussusception; the latter, in fact, is not of infrequent occurrence when marked polyposis exists. Bratrud[5] reports a case of intestinal polyposis with three distinct intussusceptions. Watts[6] also records a very interesting case of intussusception caused by these tumors which he was forced to operate on several times. At the first operation he reduced the intussusception. A week later the intussusception recurred and he resected 17 inches of the ileum which contained two tumors. Two months later he resected a portion of the colon, and at a fourth operation, three months afterward, four tumors were removed from the jejunum. Microscopically, all these tumors proved to be adenomas.

Some observers maintain that the intussusceptions in such cases are caused by the mere weight and pulling of the tumor on the intestinal wall as it is being pushed forward by the intestinal peristalsis and the stream of intestinal contents. Others, however, contend that the presence of the tumor excites violent peristalsis which causes the invagination. If the first theory were true, the tumor would always occupy the apex of the intussusception, but this is not the case.

Symptoms.—The symptoms usually vary with the position, size, and number of the polypi. Rectal polypi are usually easy to discover by proper rectal examination, and may be seen with the proctoscope. Regardless, however, of the location of the growths, they usually produce hemorrhage sooner or later. Anemia in these cases varies according to the extent of the hemorrhages. Diarrhea may become very profuse at times; rectal tenesmus may be present, and vague abdominal symptoms, as colic and obstruction, also occur. Eosinophilia may be present in this as in other intestinal conditions.

According to Doering,[1] the diagnosis can be made only when the polypus is seen or felt. He collected all the cases reported up to 1907, and out of the 52 which he reviewed, only one patient was perfectly well after four years.

Treatment.—Therapeutic treatment is useless. Depending upon the size and number of the polypi and extent of intestine involved, simple excision of the tumor itself or resection of the bowel may be necessary. In many cases the involvement may be so extensive as to preclude even surgical interference.

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THE ROENTGENOLOGIC FINDINGS IN THREE CASES OF DIVERTICULITIS OF THE LARGE BOWEL *

RUSSELL D. CARMAN

According to McGrath,[1] Graser in 1899 was the first to demonstrate the association of acquired diverticula with "isolated circumscribed adhesive peritonitis" on the colon, which had been mentioned by Virchow in 1853. Although not of common occurrence as compared with other lesions of the large bowel, diverticulitis, nevertheless, is met with sufficiently often to require its consideration in many cases with symptoms referable to the colon. Thus as early as 1907 Mayo, Wilson, and Giffin[2] were able to report 5 cases operated on in the Mayo Clinic, and in 1912 Giffin[3] collected 27 such cases, in 17 of which there was involvement of the sigmoid. Giffin has discussed the symptomatology, and only the salient features require mention here.

The proportion of males to females appears to be two or three to one. An inclination to obesity is noted almost without exception. The patients are of sound flesh, with good color, and, where loss of weight occurs, it is only slight. Abdominal pain, usually of considerable severity, is the rule. Often the patient is able to localize the pain to the sigmoid or descending colon. Constipation is complained of by the majority, and is often of more than moderate severity. Vesical symptoms, such as frequency and tenesmus, are occasionally noted. In every instance of diverticulitis of the sigmoid a mass was felt in the left lower quadrant or in the pelvis. The proctoscopic examination has been negative,

save in one case, where the tumor had become partially intussuscepted into the rectum. Absence of blood from the stools is notable, and this is explained by the fact, pointed out by Wilson,[2] that the inflammatory process is primarily extramucosal, and that the condition is really a peridiverticulitis.

Given a case with such symptoms, the differential diagnosis becomes a matter of some importance. One condition which must be eliminated is that of left-sided appendicitis. Here the roentgenologic examination would be decisive by showing the position of the cecum. The most difficult differentiation is from carcinoma. While the symptoms are not quite typical of carcinoma, they do not absolutely contradict it. Indeed, Wilson[4] has shown that carcinoma may develop within the diverticula. The question arises as to what can be expected from the x-ray.

McGrath,[1] in his very complete review of the pathology, has brought out the following facts: Nearly all these diverticula are of the "false" type, that is to say, they are hernias of the mucosa through the muscularis, commonly at points where the latter is penetrated by vessels. The chief causes are weakness of the muscularis, with an increase of intra-intestinal pressure such as occurs in stasis and gas formation. Diverticula vary in size from that of a pea to a hen's egg. They are usually round or ovoid, and most often sessile, though occasionally pedunculated. The opening into the bowel may be narrow and practically stenosed, or it may be almost as wide as the diverticular cavity. Except those in the small intestine, the sacs usually contain fecal matter and sometimes fecaliths. Histologically, the sac-wall is made up of mucosa and serosa, the muscularis being slight or wanting. The mucosa may be slightly atrophic or even ulcerated, but the most constant pathologic process is the chronic, proliferative, extramucosal inflammation, the "peridiverticulitis" of Wilson, with round-cell infiltration which results in mass-formation.

Over a year ago I examined the fixed and somewhat shrunken pathologic specimens of diverticulitis at St. Mary's Hospital with regard to the possibilities of roentgenologic diagnosis of the condition. A cursory inspection of this material gave me the im-

pression that the demonstration by the x-ray of the diverticula themselves was almost, if not quite, hopeless. The vast majority of them were far too small to be visualized, even if their filling with opaque material could be assured. The few larger ones, if capable of being filled at all, were, I thought, likely to contain fecaliths or fecal material which would prevent the entrance of the opaque enema. The next conclusion was that a filling defect could in many instances be demonstrated, but that this could not be distinguished roentgenologically from a filling defect due to carcinoma. I still held this view when the three following cases came up for examination:

CASE 1.—(99640.) Male, aged fifty-five, physician. Examined January 26, 1914. Family and personal history negative.

Previous Diseases.—Gall-stones (passed one). Severe chole-cystitis and peritonitis fifteen years ago.

Former Operations.—Twelve years ago he was operated on for left inguinal hernia and hemorrhoids.

Clinical History.—Post-operative abscess following above operation, with symptoms of cystitis. The abscess developed around the ligature later, which was passed by urethra. Since then the patient has had symptoms of bowel obstruction, the last time in December, 1913, one attack five years prior to this. There was left-sided griping and gas pains, with much distention. At one time the bowels did not move for eight days; ordinarily, however, they move regularly. Apparent lump and soreness in left iliac fossa, with pressure affecting the bladder. Pencil stools before last attack. The patient returned to his home, and prior to his operation, March 17, 1914, suffered several obstructive attacks, with flatulence, rumbling, and stinging pain over the pubis and left side during bowel movement. Sensation of "something pushing up from rectum" when in sitting posture. Some weight fluctuation, but the greatest loss at any one time was 12 pounds. Urine negative. No record of examination of blood or feces.

Roentgen Examination (Fig. 106).—January 27, 1914, patient was examined in the routine way by barium enema. Roentgenograms showed an irregular, filling defect with marked narrowing in the sigmoid. Small barium shadows were observed outside the lumen of the bowel, an appearance quite unusual, and at that time inexplicable. From the clinical facts and the Roentgen ap-

pearance W. J. Mayo suggested to the patient that the condition might be diverticulitis.

Operation.—March 17, 1914, first stage of Mikulicz for tumor of sigmoid (diverticulitis, inflammatory). Bowel exceedingly thick and adherent to pelvic wall posteriorly; about 14 inches of bowel involved. Subsequent stages performed on March 24th, April 4th, and April 24th.

Pathologic Report.—Tissue removed, sigmoid.

Diagnosis.—Diverticulitis. The patient made a good re-
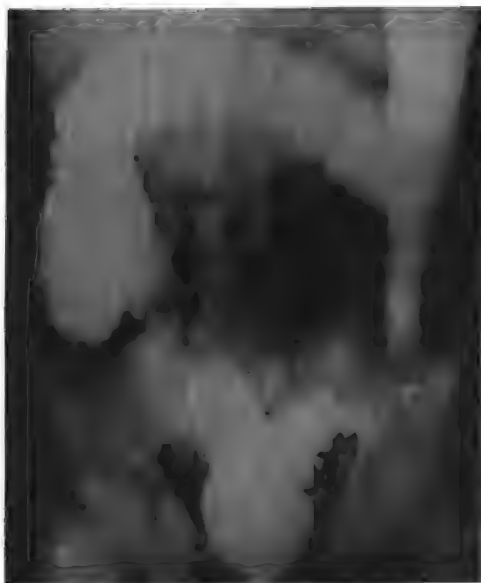
Fig. 106.—(99640.) Roentgenogram of barium-filled colon (enema), showing marked filling defect in sigmoid, with extralumenal shadows (diverticula) at *A, A.*

covery, has taken on considerable weight, and is carrying on his accustomed work.

CASE 2.—(105595.) Male, aged fifty-one, merchant. Examined May 7, 1914. Family and personal history negative. Denies any previous disease.

Former Operation.—Appendectomy elsewhere, without any exploration.

Clinical History.—For ten years he has been constipated. In the past two years he has noticed a sore lump in the left lower ab-

domen which has been associated with an increase of constipation. On two occasions this lump became swollen and very tender. In December, 1913, he had a chill with fever, and griping pain with gas, marked swelling, and soreness at the spot complained of. Recent similar attack four days ago. Stools small and tapered, necessitating laxatives, but no blood or pus noted. When the lump was swollen, the patient had frequent urination with some pain. General health good. Weight loss, five pounds.

Physical Examination.—Tenderness and resistance in lower

Fig. 107.—(105595.) Shows barium-filled colon (by enema) with extralumenal shadow (diverticula) at *A*.

left abdomen. Rounded, elongated mass felt by bimanual examination. Rectum seems negative aside from small hemorrhoids.

Proctoscopic Examination.—Negative.

Roentgen Findings (Fig. 107).—Negative save for slight enlargement of cecum. At the same time small shadows were noted outside the sigmoid lumen, but their significance was not at that time appreciated.

Operation.—May 13, 1914, first stage Mikulicz by C. H. Mayo. Diverticulitis of sigmoid. Subsequent stages May 19th, June 2d and 23d.

Pathologic Report.—Tissue removed, sigmoid.

Diagnosis.—Diverticulitis. This patient made a complete recovery and has had no trouble since. ·

CASE 3.—114002. Male, aged fifty-four, merchant. Examined August 28, 1914. Family and personal history negative.

Clinical History.—Attacks of pain and tenderness in left iliac fossa. Illness began as a diarrhea lasting several months. He has recently noticed that a full bladder causes a sensation of pressure. During the past eight months he has had indefinite

Fig. 108.—(114002.)   Colon filled with bariumized enema.   Diverticula at *A*.

gastric symptoms, with vague discomfort after meals. He is gradually losing weight and strength.

Roentgen Findings.—The roentgenogram (Fig. 108) shows a fairly normal colon save for insufficiency of the ileocecal valve and some extralumenal shadows along the inner aspect of the descending colon. This patient has not yet been operated on.

In the first case particular attention was given to the roentgenograms. These showed the filling defect of an organic lesion in the

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sigmoid, and, although the history suggested a benign inflammatory lesion, carcinoma was nevertheless considered probable from the x-ray standpoint. The shadows noted outside the sigmoidal lumen could not then be accounted for. In the second case these
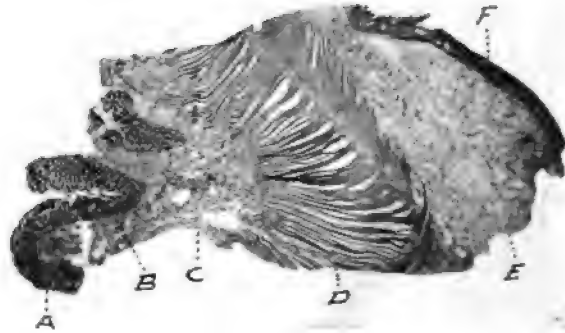
Fig. 109.—(99640.) Cross-section of wall of normal sigmoid. Photomicrograph, magnified four times, showing normal mucosal fold. Note that this fold does not penetrate the musculature. *A*, Mucosa; *B*, mucosal fold; *C*, submucosa; *D*, musculature; *E*, subperitoneal fat; *F*, peritoneum.
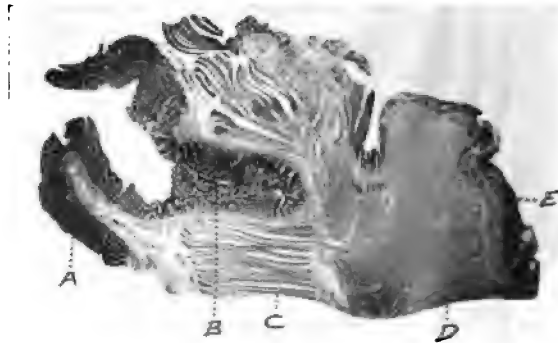
Fig. 110.—(99640.) Cross-section of wall of sigmoid. Photomicrograph, magnified four times. Shows mucosal fold and submucosa separating the circular muscular fibers and penetrating to the longitudinal musculature. An early diverticulum of this type can hardly be demonstrated radiologically because of the absence of flask-like dilatation. *A*, Mucosa; *B*, diverticulum; *C*, circular muscle-fibers; *D*, subperitoneal fat; *E*, peritoneum.

same shadows were seen, but no filling defect was observed and no interpretation was attempted. When operation showed the existence of a diverticulitis in this case also, the plates of both cases were brought out and compared, and the presence of extra-

lumenal shadows in both began to take on considerable significance. Still hampered by the preconceived idea that diverticula could seldom or not at all be vitalized, I sought some other explanation of these shadows. A colleague having suggested that they might be due to calcareous deposits, I secured the specimens, examined them, and present the results herewith.

Sections of the tissue removed from Cases 1 and 2 (Figs. 109–113) here illustrated show the customary pathologic changes. The diverticula of varying size have herniated through or partially
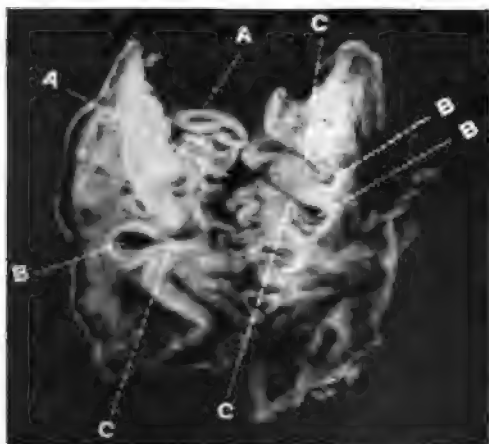
Fig. 111.—(99640.) Longitudinal section through sigmoid, showing multiple diverticula with marked thickening of intestinal wall and narrowing of lumen. *A*, Mucosa; *B*, diverticula, containing fecaliths; *C*, canal leading to diverticular sac.

through the muscularis, and lie within the greatly thickened subperitoneal tissue. Some of them contain fecaliths, others are empty. No calcareous infiltrations are anywhere present. The extralumenal shadows in the roentgenograms, which are plainly shadows of barium, correspond in contour and situation to the larger diverticula.

Notwithstanding the fact that sigmoidal diverticula are commonly filled with fecal material, it is evident from the two cases herewith shown that the sacs are not always thus filled, or may, at least in some instances, be emptied by purgation and a cleansing

enema, and, if of sufficient size, may be filled with an opaque clysma and be visualized by the Roentgen ray. When thus seen, they appear as oval or rounded barium shadows just outside the intestinal lumen, and this appearance would seem to have high diagnostic value in differentiating the condition from carcinoma. While a carcinoma might show more or less apparent pocketing, due to degenerative changes, such pockets would not have the rounded symmetry of diverticula. In the case of carcinoma supervening upon diverticulitis, which sometimes happens, if extralumenal shadows were present, the roentgenologic appearances
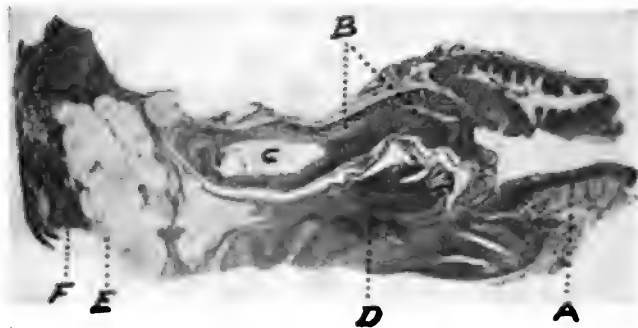
Fig. 112.—(99640.) Cross-section of wall of sigmoid. Photomicrograph, magnified four times. Deep-seated late-stage diverticulum with flask-like ampulla. The diverticulum has separated the circular fibers, which are here seen compressing the neck, passed through the longitudinal bands of muscle, and penetrated into the subperitoneal fat. This advanced type offers the greatest opportunity of radiologic demonstration because of its capacity and the distance from the intestinal lumen. *A*, Mucosa of bowel; *B*, canal leading into diverticular cavity at *C*; *D*, musculature; *E*, subperitoneal fat; *F*, thickened peritoneum.

would be those of diverticulitis, while if these shadows were not present, the case would be regarded as one of carcinoma.

To be borne in mind is the possibility that, by reason of a stenotic inlet or extremely small size of the diverticula, or by their containing fecal matter, they may fail to fill with the clysma. In this event there would be seen only a filling defect proportional to the extent of the inflammatory thickening and not distinguishable roentgenologically from that of carcinoma. As to the chance of a fecalith being seen, that would depend upon its size, density, and situation. It is also quite possible that sufficient barium may enter a diverticulum containing a fecalith to make the sac visible.

Phleboliths or calcified glands may give shadows resembling those of barium-filled diverticular pockets.   If in the region of the upper sigmoid palpation during the screen examination may show that the phlebolith or gland-shadow has no relation to the bowel, while that of a diverticulum moves with it.   If situated near the lower sigmoid, which cannot be shifted about by palpation, the distinction could not be thus made.   Hence a screen or plate examination before administering the enema might be an advisable routine to eliminate the possibility of phleboliths or calcified glands in this region.

Fig. 113.—(105595.)   Cross-section of diverticulum.   Photomicrograph, magnified four times *A*, Mucosa of sigmoid; *B*, neck of diverticulum (not well shown on account of depth at which section was cut), extending from lumen of sigmoid through circular muscular fibers to diverticular sac at *C*. *D*, Subperitoneal tissue; *E*, peritoneum.   Note that mucosal lining of the diverticulum is like that of the sigmoid, and it differs in this respect from the inflammatory pockets produced by perforating ulcer of the stomach which are often, but wrongly, spoken of as diverticula.

Since diverticula tend to occur near the mesenteric border of the bowel, in the neighborhood of the vessel entrances, they are usually best seen in the anteroposterior view.   But they may occur in other situations, and if on the anterior or posterior wall, may be obliterated in the shadow of the bowel as seen in the anteroposterior view.   For this reason both the screen and plate examination should be made at various angles of observation, and stereoscopic roentgenograms made when possible.

The rarity of roentgenologic findings in this condition can be understood from the fact that, as far as I can learn, only one case has hitherto been reported (Abbe[5]), the roentgenologic work being done by Le Wald.   It is also worthy of note that a monograph

published this year by G. Schwartz,[6] of Vienna, on the Roentgen diagnosis of the colon, makes no mention of diverticulitis.

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INTESTINAL PARASITES OF MINNESOTA *

A. H. SANFORD

The bacterial flora of the intestinal tract is not usually con-
sidered in the study of parasites, nor do I wish to cover the field
of animal parasites in this discussion, but to confine myself to the
protozoa that have been found in the stools of patients residing
in the state of Minnesota. Within the past three years there have
been 133 residents of this State examined in our Clinic in whom one
or more parasites of this character have been found.

The method of making a stool-examination for intestinal pro-
tozoa may be worthy of mention. The matter of diet is of no
particular consequence. The patient is instructed to take one-
half to one ounce of Epsom salts in the morning before eating,
and then go to the laboratory for a stool. This is collected, free
from urine, in a suitable container, and examined at once. A
cover-slip preparation is made from the stool, and a simple warm
stage used to keep the material at body temperature while the
search is made for motile parasites (Fig. 114). It cannot be em-
phasized too strongly that stools an hour or so old, and not follow-
ing salts, are of no value whatever in a search for amebas.

The flagellates are found very frequently in stool-examinations.
It is doubtful whether they are of much pathologic significance.
Of this group, the most common is Trichomonas intestinalis. The
following description is from Braun[1]:

Class II. Flagellata (Mastigophora).
A. Polymastigina.

Genus I. Trichomonas. (Described by Donné,[2] 1837.)

"The body is generally pyriform, the anterior part usually rounded, the posterior part pointed. There are three or four equally long flagella that are sometimes fused. In addition, there is an undulating membrane that commences at the anterior extremity and proceeds obliquely backward. The nucleus is situated at the anterior extremity; and behind it are one or more vacuoles, none of which seems to be contractile. These flagellates are parasitic in vertebrate and in invertebrate animals, and live chiefly in the intestine."
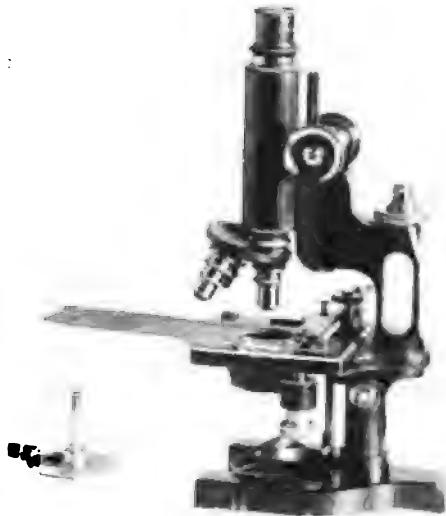
Fig. 114.—Microscope fitted with simple warm stage.

This organism infects the vagina at times and has been named by Donné Trichomonas vaginalis. It is, however, probably identical with the parasite found in the intestinal tract, which is called Trichomonas intestinalis. We have seen this organism occurring 25 times with other parasites, and thirty times alone in patients from this State.

Opinions differ as to the importance of this parasite. Most text-books on laboratory diagnosis have perpetuated the old idea

that they are non-pathogenic. In 9 of the 30 cases in which nothing but trichomonads were reported there was no diarrhea, but rather constipation; however, 12 patients had constant diarrhea, and 9 complained of intermittent attacks of bowel trouble, and many of them had blood and mucus in the stools. It is hard to say, then, whether this organism is entirely harmless. Even if not an etiologic factor, it, or its waste products, may possibly act as an irritant to mucosa inflamed from some other cause. Its habitat is the small intestine; and it is not an easy matter to drive it from the alimentary tract.

Another organism of this same group belongs to the genus known as Lamblia. Stiles[3] says that its "body is bilaterally symmetric, pyriform, excavate anteroventrally to form a sucker; flagella directed posteriorly; three pairs inserted on margin of the sucker, one pair at posterior end of body. Parasitic in intestine of mammals."

The species found in man is called Lamblia duodenalis or intestinalis, and is probably identical with, or very closely related to, Lamblia muris, found in the intestines of rats and mice. This has suggested the probability that man is infected by eating food that has been contaminated by these animals. The parasite inhabits the small intestine, and attaches itself to the mucosa by means of its sucking orifice. Like trichomonas, it has been called a harmless parasite. Stiles, however, is inclined to the belief that a heavy infection may be the cause of real disturbance. Stitt[4] says on this point: "This parasite is considered of little importance, but as it is responsible for a chronic and intractable diarrhea, associated with mental and physical depression, it undoubtedly causes an affection minor in importance only to amebic infection."

There were four cases from Minnesota in which we found Lamblia intestinalis. All the patients were suffering from chronic diarrhea, but only two of them had lamblias as the only parasite. One of these cases had been in the State Asylum for thirteen months. It has been noted that patients in institutions are apt to have parasitic troubles. Two of the cases were associated with entamebas of a pathogenic type, the patients exhibiting severe

symptoms. One of them, a Russian Jew who had never been south nor in the tropics, had a large liver abscess which may have been of amebic origin.

In 15 Minnesota patients Cercomonas hominis were found, 6 times associated with amebæ and 9 times alone. This organism belongs to Group B of the flagellates, the protomonadines, and is much smaller than the trichomonad. It has a pear-shaped body elongated into a terminal flagellum posteriorly, and has one anterior flagellum. It has no undulating membrane, and darts quickly about the field, quite unlike the peculiar slow movement
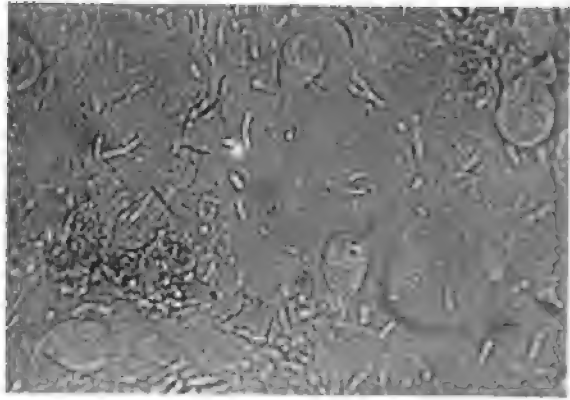
Fig. 115.—Microphotograph of Lambliæ intestinalis.

with which trichomonas propels itself forward. Its status as regards pathogenicity is practically that of trichomonas.

The fact of most importance which has developed from a routine examination of stools in patients with chronic diarrhea is that in some of these cases amebas of a pathogenic type may be demonstrated; and treatment along these lines relieves the patient of his distressing symptoms. Sistrunk,[5] in his report of the stools examined three years ago, reported 12 instances of pathogenic amebas found in patients who had never been south. A few of these were residents of Minnesota. Since then, and including Sistrunk's examinations, which covered four and one-half months,

we have found in Minnesota patients amebas of the pathogenic type 28 times, and 65 cases of infection with a type that is usually considered non-pathogenic. The most common intestinal protozoön that we find is some type of ameba.

Intestinal amebas belong to the type of naked ameba, or Gymnamebida. Lambl,[6] in 1860, noted their presence in the stools of a child with diarrhea. In 1875 Loesch[7] described them, and called the organism Amœba coli. Four years later Grassi[8] reported amebas in the stools of a healthy individual, and he considered them of no importance. In 1886 Kartulis[9] found amebas present

Fig. 116.—Microphotograph of Entamæba histolytica.

in the stools of patients with Egyptian dysentery. In this country Councilman and Lafleur[10] reported, in 1891, that they believed that amebas were the cause of dysentery in our southern States. The name "entameba" was suggested in 1897 by Cassagrandi and Barbagallo[11] for the type found in man. It was not until 1903, however, that a thorough study of these parasites was made by Schaudinn.[12] He concluded that there were two types—one pathogenic and one non-pathogenic. The latter he named Entamœba coli; and because of its tissue-destroying powers, he called the pathogenic organism Entamœba histolytica. In 1907 Viereck[13] and also Hartmann,[14] working independently, described in detail

the reproduction stages of a dysentery-causing ameba, which, in encysting, formed four daughter-cells. This ameba was called by them Entamœba tetragena.

Craig[15] has written very completely from time to time on parasitic amebas in man. We have tried to follow closely his descriptions in classifying the active unstained ameba as found in fresh stools. The morphologic characteristics are as follows:

Entamœba coli is usually round, with a readily seen central nucleus. The ectoplasm is clear, so that the structures of the endoplasm are easily seen. The pseudopodia are very small—
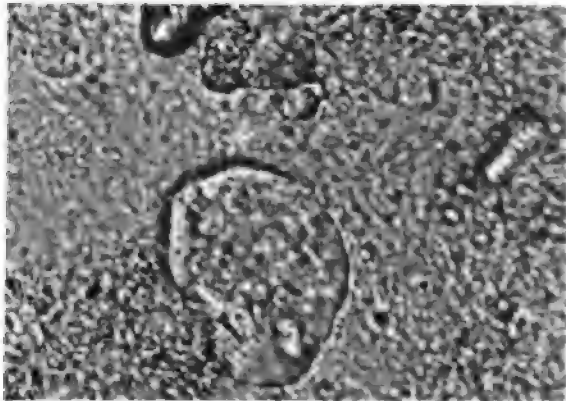
Fig. 117.—Microphotograph of Entamœba histolytica.

merely slight bulgings of the ectoplasm. Motion is sluggish. Encysted forms show eight daughter-cells.

The form of pathogenic ameba described by Schaudinn as Entamœba histolytica is irregular in shape, has a thick, hyaline ectoplasm, so that the nucleus and other structures of the endoplasm are not easily seen. It moves rapidly, and pushes out finger-like, lobose pseudopodia.

Entamœba tetragena is irregular in shape, but, because the ectoplasm is clear, the differentiation is marked between the inner and outer structures as the organism pushes out its long, finger-like or lobose processes. The nucleus is eccentric and easily

studied. Red blood-cells are ingested, and when digested may give rise to the peculiar greenish tinge of the organism seen at times. Cysts are seen containing but four daughter-cells.

Within the last year, however, a number of men have come to the conclusion that Entamœba histolytica and Entamœba tetragena are the same organism. Darling[16] holds that, since the reproduction is evidently by four daughter-cells, it should be called *tetragena*. Craig replies, and with reason, that Schaudinn was right as to its pathogenicity, and that the name given by him, *histolytica*, has priority, and describes the organism, even if he did study a degenerating form rather than one showing reproducing stages.

I believe this organism to be much more common in the northern States than is ordinarily thought. The distribution of cases with both pathogenic and non-pathogenic amebas throughout the State seems to be of little significance. There are more cases from southern Minnesota, but there are more patients coming to the Mayo Clinic from these regions. In a few instances there are several cases from the same locality, but there is no apparent reason for tracing one case to another.

The clinical symptoms of amebiasis are not so marked in northern climates, as a rule, as in patients in the tropics. Seven cases of chronic constipation showed amebas morphologically pathogenic. The usual complaint was intermittent attacks of diarrhea, in several instances accompanied at times with blood and mucus. Five patients reported constant diarrhea. The average number of stools a day is three to six. Pain is a common complaint, often of an indefinite sort, but in other instances well localized. A few more cases gave a history of pain over the splenic flexure than at the hepatic flexure or the cecal region. No pain at all was reported in 6 cases, while 14 patients had no tenderness on pressing the abdomen in physical examination.

The question often occurs to us, "What is the source of the infection?" "Has every case contracted the disease from some one carrying the parasite?" "Is some domestic animal an inter-

mediate host?" We have not been able as yet to throw much light on this phase of the subject. The history as to water-supply is not conclusive. Every one may some time drink impure water. In all our cases less than one-half give deep-drilled or artesian wells as the source of their water-supply. Such water ought to be pure. More than one-half, however, were drinking from shallow wells, springs, cisterns, lakes, or streams.

Sistrunk found Balantidium coli in one Minnesota patient, a male forty-two years of age, who had never been south, and who had contracted diarrhea twelve years ago in Wisconsin. He became much worse afterward in Canada when he was drinking water from an impure source. At the time of his examination he was losing weight and had diarrhea at intervals. It was found that he had an anemia of the pernicious type. There were large numbers of balantidia reported in his stools. Eight months later the patient returned for examination, and was found to be much improved, with no balantidia in the stools. He had gained in weight and strength, and the condition of his blood was much improved. We have not heard from him since. This parasite belongs to Class IV, Infusoria, the second order, Heterotricha. It is oval in form, and has a peristome surrounded by stout cilia. There is a large macronucleus and also a micronucleus. It moves rapidly with a peculiar darting motion. Encysted forms are typical. A somewhat similar organism, Balantidium minutum, is found quite commonly in the hog's intestinal tract. Balantidium coli is considered pathogenic by observers in the tropics, producing severe ulceration which may lead to a fatal termination.

It is generally thought that the protozoa of the intestinal tract are of little interest except to the student of tropical medicine. We believe, on the other hand, that amebic dysentery is a universal infection; and though it may not be found in its severe forms in northern States, yet it is of enough importance to warrant a careful diagnosis. A stool-examination is a simple procedure when properly carried out, and may result in findings which will lead to the relief of a chronic and distressing ailment.

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UROGENITAL ORGANS

THE PRACTICAL VALUE OF CHEMICAL TESTS OF RENAL FUNCTION IN SURGICAL CONDITIONS OF THE URINARY TRACT *

WILLIAM F. BRAASCH AND G. J. THOMAS

The practical value of an estimation of renal function by means of chemical tests has not as yet been definitely determined. Medical literature during the past decade has been replete with articles concerning this subject. With the advent of each of the various functional tests it was believed that the means had been discovered whereby an exact estimate of renal function was possible. In 1909 the use of phenolsulphonephthalein as a renal functional test was advanced by Rowntree and Geraghty, who claimed that in its use many of the objectionable features of other tests had been overcome. Since then many articles have appeared, largely corroborative of the claims of Rowntree and Geraghty. As a result, the general impression now in this country is that an estimation of renal function by means of chemical tests is necessary before any surgical procedure can safely be made in the urinary tract.

In our experience phenolsulphonephthalein undoubtedly embodies many of the virtues which the various other tests lack. Since phenolsulphonephthalein is representative of underlying fallacies common to all functional tests, its use will be illustrative of the practical value of such tests. In an effort to determine its practical value when applied to surgical conditions of the urinary tract we have employed it in 612 cases. In reviewing these tests

they have been studied in regard to their value when applied to the following conditions: (1) For the purpose of determining the efficiency of the remaining kidney. (2) The estimation of renal functional capacity in cases of urinary obstruction. (3) As an aid to the diagnosis of doubtful lesions of the kidney.

In the literature on the subject of renal functional tests the statement is frequently made that the greatest danger in renal surgery is insufficiency of the other kidney. Rowntree, in a recent article, says: "Uremia after operation has been responsible for a large proportion of the mortality in surgical cases." This observation, however, has never been proved by an extensive survey of a large series of operated cases. Of the 485 patients upon whom nephrectomy was performed at the Mayo Clinic during the past five years (June 1, 1909, to June 1, 1914), 19 died as the result of the operation. A review of the postmortem findings in these cases showed that renal insufficiency was the cause of death in but one case where a complete cystoscopic examination was made prior to operation. In this patient a nephrectomy had been made for unilateral renal tuberculosis. Although the clinical symptoms prior to operation were suggestive of renal insufficiency, the operation was made for relief of acute pain referred to the affected kidney. In two other cases the remaining kidney was insufficient because of tuberculous infection. Because of difficulties in cystoscopic technic, neither of these kidneys could be catheterized. On surgical exploration the remaining kidney appeared to be in fair condition, but at autopsy was found to be practically functionless. In one of these cases the combined phenolsulphonephthalein output in two hours was 38 per cent. prior to operation. A review of the autopsy data would lead us to believe that the cause of death following renal surgery will more often be the result of infections and possible errors in surgical technic than of insufficiency of the remaining kidney.

It is a well-known fact that when one kidney is diseased the functional activity of the other kidney may be temporarily reduced. The degree of reduction may be so marked as to suggest an actual lesion. The degree of functional reduction, however, is not neces-

sarily commensurate with the extent of actual destruction of tissue. The fundamental weakness of all renal functional tests as an aid to prognosis is that while they may show the degree of functional activity at the time of examination, one cannot determine from them what the functional capacity may be when the existing pathologic conditions are corrected. It has been our experience that the fundamental surgical principles and the clinical data, including a careful cystoscopic examination, are to be relied on in determining whether or not a patient should be operated upon. In other words, if a surgical condition is present in one kidney, operation is indicated provided there is a fair amount of clear urine in the catheterized specimen of the other side and that the patient does not give evidence of the well-known clinical symptoms of renal insufficiency.

Urinary Obstruction.—We have employed the phthalein test in 168 cases of prostatic hypertrophy. In the majority of cases the test was repeated at regular intervals in order to note the degree of comparative progress. It has been claimed that, with a persistent low output of phenolsulphonephthalein, in spite of treatment we have evidence of renal insufficiency which would contraindicate operation. While it would probably be impossible to set any arbitrary percentage as the operative danger line, it is generally understood that a 20 per cent. return in two hours might be so regarded. Our series includes 11 patients operated on, with an output of less than 20 per cent., all of whom had repeated examinations and long-continued treatment. Of these 11 patients, but one died, evidently from cardiac rather than from renal insufficiency. In two patients, even after months of treatment, the return in two hours was so slight as to be scarcely measurable, and yet both made uneventful recoveries—one of whom two years afterward is reported in excellent health. On the other hand, two patients with a phenolsulphonephthalein output of 30 and 45 per cent. respectively, after treatment of the bladder died with clinical symptoms of uremia, and several patients with an output of over 40 per cent. prior to operation developed uremic symptoms after prostatectomy, but finally recovered.

In 9 patients the phenolsulphonephthalein output was over 75 per cent. in two hours. Of these, 2 died following operation, 1 died with clinical evidence of uremia and a pathologic diagnosis of nephritis, largely glomerular, in both kidneys. The other died with evident cardiac dilatation, and the pathologic examination of both kidneys showed a chronic parenchymatous nephritis.

It has been claimed that successive tests are necessary to establish the functional capacity, and that only when the amount of dye secreted increases progressively is the efficiency of renal function established. Of the 10 cases operated upon with an output of less than 20 per cent., the amount remained practically stationary throughout treatment. In several cases the secretion had been around 20 per cent. after the first reaction to treatment, then rose to 30 per cent., but dropped to 20 per cent. or even less prior to operation. We have concluded that, although the amount secreted usually increases after drainage and treatment of the bladder, a stationary or even decreasing output should not influence the prognosis, provided the patient's general condition is improving.

Of interest is a review of the specific gravity of the urine. While, as a general rule, a drop in specific gravity was accompanied by a drop in the phenolsulphonephthalein output, there was no certain degree of parallelism between the two tests. Thus of 63 patients in whom the phenolsulphonephthalein output was over 50 per cent., in 32 the specific gravity remained lower than 1010. On the other hand, of the 11 cases with less than 20 per cent. phenolsulphonephthalein output 9 had a specific gravity of less than 1008. It has been our experience that the specific gravity, when repeatedly ascertained in the course of preliminary treatment, was fully as valuable in an estimation of the patient's renal activity as any of the various functional tests.

We believe, however, that the clinical evidence of renal insufficiency after the usual course of treatment is of greater importance than any functional test, and should determine whether or not prostatectomy is indicated. That we are correct in our observation is proved by the fact that recently a series of 97 prostatectomies was performed at the Mayo Clinic without a death.

Probably the greatest value of the functional test will be as an aid to the diagnosis of doubtful lesions of the kidney. For this purpose phenolsulphonephthalein is admirably adapted. The presence of a marked diminution of dye-secretion on one side should be regarded as indicative of the existence of some pathologic lesion. Its absence, however, will not exclude the possibility of the existence of a lesion. Unfortunately, technical difficulties accompanying ureteral catheterization are frequently the cause of error in the functional estimate, and in order to corroborate the findings it may be necessary that the patient undergo repeated examinations. Slight differences in the functional output between the two kidneys are not of much practical value. To be of much diagnostic significance the comparative difference in the functional output must be marked. The phenolsulphonephthalein test is frequently of considerable value when applied in the diagnosis of renal lithiasis, ureteral lithiasis, hydronephrosis, renal tumor, renal tuberculosis, renal infection, bilateral cystic kidney, essential hematuria, and atrophic kidney.

Renal Stone.—When stone is present in a kidney, a comparative diminution in the functional output will be found in the majority of cases. It will be found in practically every case in which the stone is of considerable size and there is marked destruction of renal tissue. It will frequently happen, however, where the stone is small and where there is little or no infection that the diminution in secretion will not be enough to be of diagnostic value. Since shadows in the radiogram of stones of this type particularly require identification, the practical value of the functional test as an aid to their identification will be found to be limited. The absence of any diminution of dye-secretion, therefore, will not exclude the possibility of a stone being present.

The degree of diminution of the phenolsulphonephthalein output will not be found to be commensurate with the degree of destruction of renal tissue. As a rule, the degree of diminution in functional output will be much greater than the actual destruction of tissue. Thus in several recent cases of stone in the kidney the functional output of the affected kidney was but 1 or 2 per cent.

in fifteen minutes, while in the other kidney it amounted to 10 or 15 per cent. At operation the affected kidney was found to be practically normal. Following the removal of the stone the renal function returned to normal. From this it must be inferred that the reflex irritation from stone will frequently be the cause of temporary diminution in renal secretion.

With bilateral nephrolithiasis the test may be of value in determining the comparative degree of renal obstruction. If but a trace of the dye returns from one kidney, the destruction of tissue has probably progressed to such a degree that nephrectomy usually is indicated—a particularly valuable procedure when the urine is not markedly purulent. In one case, however, of bilateral nephrolithiasis the same amount of dye was secreted from both sides. At operation one kidney was found to be so much destroyed that nephrectomy was necessary, while the other was in comparatively good condition. If, with bilateral nephrolithiasis, but a trace of phenolsulphonephthalein is present in the combined urine two hours after injection, the advisability of operation would be questionable. Two such patients came under our observation. In one, operation was refused because of clinical evidence of renal insufficiency and toxemia. The other was operated on and was reported alive six months later.

Stone in the Ureter.—Marked diminution in phenolsulphonephthalein secretion on the side of a doubtful ureteral shadow would indicate that the shadow in question was intra-ureteral. Unless there is considerable dilatation of the renal pelvis, or infection as a result of stone in the ureter, marked diminution will not usually be found. As with renal lithiasis, stones in the ureter giving doubtful shadows in the radiogram are usually small and more often cause but little dilatation or infection in the kidney: consequently, diagnostic diminution in secretion will be found of practical value in but a small proportion of ureteral stones. An equal comparative function, however, would not exclude the possibility of stone in the ureter. In eight cases of stone in the ureter in which the secretion of the urine was not interfered with and the radiographic and

cystoscopic evidence was doubtful, positive diminution in comparative secretion was found in two cases.

Hydronephrosis.—With hydronephrosis of any considerable size a marked diminution of function occurs. This is to be explained partially by the fact that the retained fluid in the sac may dilute the dye secreted to such a degree as to give the impression that the secretion is diminished. It will frequently be quite impossible to remove all the retained fluid by means of the catheter, so that the functional test will have but little exact value in estimating the degree of renal destruction. As with lithiasis, the degree of tissue destruction is not parallel with the degree of diminution of functional output. With a very small hydronephrosis, however, in which a functional test might be of practical value, but little difference in secretion may be found in the two kidneys since the parenchyma is usually but slightly involved.

Renal Tumor.—When the classic symptoms of hematuria, pain, and tumor are present, and a thorough cystoscopic examination is possible, the condition of renal tumor can usually be readily recognized. Renal neoplasm, however, will frequently occur without any urinary symptoms, and examination of the urine catheterized from both kidneys may be found to be normal. In such cases a marked diminution of the amount of dye secreted by the side in which the tumor in question is situated would suggest its intrarenal nature. In 29 cases of renal neoplasm in which the phthalein was employed marked diminution was found in 9. With infected neoplasm, the proportion of kidneys with tumors showing a diminution in secretion would be greater. However, the cystoscopic evidence of infection from the side of the tumor would usually render a diagnostic functional test unnecessary.

Essential Hematuria.—In the 14 cases of essential hematuria in which the phenolsulphonephthalein test was successfully employed no marked comparative diminution of dye-secretion from the hemorrhagic kidney was noted. If there is any diminution of dye-secretion in the kidney from which the hemorrhagic urine is secreted, some condition, other than the so-called essential hematuria, is present and surgical exploration is indicated. The other

conditions which may cause hematuria can usually be ascertained by the various other means of investigation at our command. Nevertheless, the method will not infrequently be applicable in the differential diagnosis of hematuria accompanying the following conditions: (1) Renal tuberculosis of the hemorrhagic type without other clinical or cystoscopic evidence. (2) Renal neoplasm which causes no recognizable tumor. (3) Renal stone with negative x-ray findings. (4) Chronic pyelonephritis. It must, however, be remembered that any one of these conditions may be present even though no marked diminution in function is apparent. The technical difficulties accompanying ureteral catheterization as the result of marked hematuria will frequently render the comparative functional estimate unsatisfactory.

Atrophic Kidney.—The only condition in which an estimate of the secretory capacity of the kidney by means of cystoscopic inspection and ureteral catheterization might be incorrect would be with an atrophic renal condition, as Geraghty has demonstrated. Atrophy of the renal substance to a variable degree is not an uncommon condition. In a series of 81 kidneys removed at postmortem and at operation which showed a variable degree of atrophy Simpson, of the Mayo Clinic, found that the condition was due to inflammatory changes in practically every case. Atrophy of the kidney which could not be accounted for by secondary inflammatory change was not found in this series. When a cystoscopic examination was made, attention was usually called to the condition by the absence or marked diminution in amount of the secretion or by the gross character of the urine secreted from the affected kidney. In two cases in which a surgical condition was present in one kidney a clinical diagnosis of insufficiency of the other kidney was made from very apparent clinical evidence of renal insufficiency. This leads us to believe that a condition of atrophy in a kidney to a degree that it will not sustain life, when the only evidence of its existence can be ascertained by demonstrating that but a trace of the injected dye returns, while possible, must be exceedingly rare. With a surgical kidney on one side and a markedly atrophic kidney on the other, the clinical evidence

of renal insufficiency alone will usually render the case inoperable. Data ascertained through cystoscopic examination will, with rare exceptions, give us the necessary corroboratory evidence.   That we are correct in our premises is proved by the fact that, among the 485 cases in which nephrectomy was done, atrophic kidney was never found as the cause of death.

Renal Infection.—Geraghty has called our attention to the fact that the phenolsulphonephthalein test is frequently of practical value in differentiating between an infection largely involving the renal pelvis and one which affects the renal parenchyma to a marked degree.   Occasionally, an infection with a low functional return will become practically normal after treatment.   With bilateral pyelonephritis, however, the phenolsulphonephthalein output will frequently remain practically normal, and still the patient may give unmistakable clinical evidence of renal insufficiency.   Two patients were observed with a bilateral colon infection in whom the first phenolsulphonephthalein output was 13 and 15 per cent. respectively.   After treatment the infection was greatly reduced, and, with the improvement of clinical symptoms, the phenolsulphonephthalein increased to 36 and 46 per cent. With bilateral pyelonephritis a marked diminution in phenolsulphonephthalein secretion from one kidney would indicate considerable destruction of kidney tissue.   With hematogenous septic nephritis, marked diminution from the kidney affected should be expected.   It was found markedly diminished in one case in which it was tried.

Renal Tuberculosis.—In the diagnosis of early tuberculosis where the tubercle bacilli have been demonstrated in the mixed urine and where cystoscopic examination and ureteral catheterization are unable to localize the disease, a marked comparative diminution of phenolsulphonephthalein on one side should localize the disease to that kidney.   In one case which came under our observation in which a circumscribed tuberculous process was present in the kidney the difference in secretion between the two kidneys was practically negative.   When, because of technical difficulties, it is impossible to catheterize only the diseased kidney

and the character of the secretion from the other side cannot be determined, as not infrequently happens in a tuberculous bladder, if the combined phenolsulphonephthalein is over 40 per cent., one might usually infer that the other kidney is.healthy. We have observed, however, one case of well-advanced bilateral tuberculosis where the combined phthalein output was 66 per cent. in two hours. On the other hand, we have noted several cases of unilateral tuberculosis where the combined phenolsulphonephthalein secretion in two hours was between 25 and 35 per cent. prior to operation. Following nephrectomy, the patients made uneventful and complete recoveries, and in one case the function rose to 60 per cent. three months after operation. It has been claimed that the phenolsulphonephthalein test is of considerable value in cases of bilateral tuberculosis where it is impossible to determine, from the character of the secretion, which of the two kidneys is more diseased. Removal of a tuberculous kidney in bilateral tuberculosis is indicated, as a rule, only when one kidney is practically destroyed and the other slightly involved. It has been our experience that if, on cystoscopic examination, one is unable to determine from the character of the urine secreted which of the two kidneys is largely destroyed, operation is contraindicated.

Perinephritic Abscess.—Marked comparative reduction in function may be the only evidence present to identify the origin of a mass palpable in the perirenal area. Perinephritic abscess of renal cortical origin may be present without any pathologic evidence in the usual examination of the urine. Marked diminution in secretion of phenolsulphonephthalein was noted in two cases of perinephritic abscess where the catheterized urine was negative save for an occasional pus-çell. In one case, however, there was no appreciable diminution present. From this it may be inferred that a perinephritic abscess may be of renal origin in spite of equal functional output.

Polycystic Kidney.—A marked diminution in phenolsulphonephthalein secretion occurs with polycystic kidneys only when the destruction of renal tissue has advanced to a considerable degree. When the disease is well advanced, clinical evidence of renal in-

sufficiency is usually manifest. In 7 cases of polycystic kidney a phenolsulphonephthalein secretion of less than 40 per cent. occurred in but two cases. In two cases a comparative reduction in phenolsulphonephthalein excretion proved to be of considerable value, however, in determining in which of the two kidneys the greater degree of destruction had taken place. This may not always be ascertained by the comparative amount nor character of the urine collected from the individual kidneys.

In conclusion, we should like to emphasize that it is not our purpose to belittle Geraghty and Rowntree in their thoroughly scientific efforts to establish a chemical estimate of renal function. The phenolsulphonephthalein test, because of the ease of application and rapidity of secretion, remains as probably the best functional test at our command. Nor is it our purpose to detract from the value of a careful examination of the character of ureteral secretion in surgical conditions of the upper urinary tract. It is our contention, however, that the fundamental surgical principles and clinical data should determine whether or not an operation is indicated; and that renal functional tests are of practical value largely as an aid to differential diagnosis and only to a limited degree as a prognostic aid.

CLINICAL NOTES ON HYDRONEPHROSIS [*]

WILLIAM F. BRAASCH

By the term hydronephrosis is designated a condition characterized by ureteral obstruction, with consequent mechanical distention of the renal pelvis. The ureteral constriction may be due to a great variety of causes which may be grouped under two general headings—namely, congenital and acquired. It is my purpose to take up for discussion the form of hydronephrosis which is caused by obstruction to the upper ureter, largely dependent upon congenital conditions. This type of hydronephrosis is to all practical purposes a clinical entity, and is called intermittent hydronephrosis.

The subjective symptoms accompanying intermittent hydronephrosis are, as a rule, not of definite localizing nor diagnostic value. However, there are three features which are peculiar to this condition and which are worthy of note, e. g.: (1) The early adult stage; (2) the periodicity of attack; and (3) the absence of urinary symptoms.

The Early Adult Stage.—In the 116 patients with intermittent hydronephrosis that have been operated on in the Mayo Clinic the average age when symptoms first appeared was twenty-one, the majority showing their first symptoms soon after attaining their full growth. This would tend to place the character of the obstruction on an anatomic basis.

Periodicity of Attack.—Practically in all the cases the appearance of the attacks, while variable, had a certain degree of regularity. The length of the intervals between the attacks usually

shortened as the condition progressed, and in the intervals the patients were free from symptoms. A constant dull pain was noted only in the later stages of the disease, and then usually in cases of secondary infection.

The Absence of Urinary Symptoms.—Although hydronephrosis may have been present many years, but few patients complained of urinary symptoms, the absence of which is of value in differentiating the condition from pyonephrosis and from lithiasis. The presence of gross pus was noted in 12 patients (10 per cent.). The absence of microscopic pus was noted in 16 patients (14 per cent.). The localization of the pain, while referred more often to the kidney area, may be referred to the anterior upper quadrant or even as low as the umbilical level. The differential diagnosis of hydronephrosis from disease in the gall-bladder and appendix is frequently impossible from subjective symptoms alone. Of the 116 patients, 51 (44 per cent.) had had previous abdominal operations elsewhere for relief of the abdominal pain.

Objective Symptoms.—On physical examination the only data of value would be in the determination and identification of tumor in the lateral upper abdomen. Our clinical records show that tumor was definitely palpable in the abdomen in 38 cases (32 per cent.). In determining the existence of abdominal tumor, however, there are many possible sources of error, among which may be considered the following:

1. Tumors of the surrounding organs so frequently simulate renal tumor in position, form, and consistence that it is quite impossible to differentiate them by means of palpation alone.

2. Renal tumor may be very uncertain on palpation when the kidney lies high and in a fat abdomen. It is frequently astonishing to find so large a tumor at operation when, on palpation, an enlargement could not be determined or was considered questionable.

Kidneys otherwise normal are occasionally so large that they simulate tumor on palpation. This is particularly true in thin patients and in the low-lying kidney.

The typical large hydronephrosis which causes tumor in the

kidney area is usually smooth and cystic and more or less movable. Occasionally, however, such a tumor may on palpation appear to be solid, irregular, or fixed. Its nature would further be concealed if it appeared without any previous subjective pain.

The clinical identification of abdominal pain and of tumor, referred to the upper lateral abdomen, is so uncertain that we are usually compelled to refer to cystoscopic examination. The diagnosis of the intermittent hydronephrosis is largely a problem of cystoscopic technic. Not alone is the diagnosis gained by this means, but the functional capacity of the affected kidney, the extent of the distention, and the condition of the remaining kidney may also be ascertained. The data to be gained on cystoscopic examination are those derived by means of—(1) Inspection; (2) the ureteral catheter; (3) the overdistention, and (4) pyelography.

Inspection.—With early hydronephrosis the data to be gained on inspection of the ureteral meatus would be of little or no value. When, however, the condition is advanced, we may expect to find atrophy of the muscle around the meatus. Further, with the decrease in renal function there would be comparative diminution of secretion from the affected side. With secondary infection, purulent urine may be seen.

Ureteral Catheter.—Although obstruction to the ureteral catheter is usually met with, in early hydronephrosis little or no obstruction may be noted. With advanced hydronephrosis, however, there will be obstruction in practically every case. By means of direct catheterization the character of the obstruction may often be felt at or just below the ureteropelvic juncture. The obstruction, even though quite definite, will, after more or less manipulation, usually permit the catheter to glide by.

When the catheter has entered the pelvis of the kidney, the next point of importance is the demonstration of the presence of residual urine. Its presence is revealed by a rapid flow of urine beyond the point of constriction without the usual peristaltic hesitation. The amount of residual urine varies with the degree of distention. Care should be taken, however, to differentiate this

rapid flow from the hypersecretion seen from reflex nervous irritation. The latter may be recognized when the flow is rapid from both kidneys. The residual urine with a hydronephrosis of considerable size is usually of low specific gravity and pale. ·

The amount of residual urine may sometimes be ascertained by suction by means of a syringe, and frequently several ounces of fluid may be withdrawn from the pelvis by this method. Care should be taken, however, that the fluid is not drawn up the ureter from the bladder.

Overdistention Method.—That the capacity of the renal pelvis can be estimated by measuring the amount of fluid injected necessary to cause pain was first suggested by Kelly. This method has received wide recognition and is still regarded as a valuable method of diagnosis in hydronephrosis, though recently its limitations have been recognized. Its greatest value is in the diagnosis of moderate degrees of hydronephrosis, of distentions with the capacity of an ounce or more. With a small hydronephrosis, however, the method has not proved to be of accurate value. With a hydronephrosis of a capacity of from 15 to 30 c.c., great difficulty would be met in differentiating it from the large normal pelvis. Various observers have noted the possibility of injecting between 15 and 30 c.c. of fluid into a large normal pelvis. This does not necessarily indicate that the renal pelvis itself has such a capacity; a part of so large an amount of fluid will undoubtedly distend the upper ureter around or above the catheter as well, which is capable of considerable distention normally before pain is caused. It would be quite impossible to estimate the amount of fluid in the ureter and pelvis separately. Therefore, if 25 c.c. were injected before causing pain, we should be unable to determine whether we were dealing with a pelvis of 7 c.c. normal capacity dilated to three or four times its normal size, or with a normal pelvis and ureter of 25 c.c. capacity.

The similarity of pain caused by overdistending the renal pelvis with that originally complained of by the patient may occasionally be of value. If the patient complains that the overdistention pain is similar to the pain felt before, this fact cannot be given much

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reliance; if, however, the patient is quite definite in saying that the pain is different from the original pain, the symptom may be of differential value.

Pyelography.—Rendering the outline of the pelvis opaque to the x-ray by means of an injected opaque solution, a method known as pyelography, has recently been employed to advantage. It has been proved to be of greatest value in the diagnosis of early hydronephrosis. It may be of value also in determining the existence, degree, and character of moderate hydronephrosis, but it is distinctly contraindicated in the diagnosis of large hydronephroses.

Early Hydronephrosis.—Probably the first deviation from the normal to be noted with early hydronephrosis is a flattening of the terminal irregularities seen in the normal minor calices. Accompanying the shortening of the minor calix there is usually a broadening of the entire calix, particularly at its base. Following soon or accompanying these changes will be noted an increase in the size of the true pelvis. With the increase in size of the pelvis, a shortening or flattening of the papillæ projecting between the calices is noted. The greatest difficulty occurs in differentiating early hydronephrosis from the large normal pelvis, since not infrequently the true pelvis of a normal kidney is of unusual size. However, if on close inspection it is seen that the terminal irregularities of the minor calices are well preserved, and there is no broadening of the base of the calices, hydronephrosis would be definitely excluded. The changes from the normal must be well marked in order to identify the hydronephrotic condition. When any doubt arises as to whether a pelvis is abnormally enlarged, it may be of value to make a pyelogram of the pelves of both kidneys and compare the outlines. As a rule, an unusually large but otherwise normal pelvis occurs bilaterally. With the outline of the pelvis on one side appearing two or three times as large as that on the other, we should have corroboratory evidence of pathologic distention.

Moderate Hydronephrosis.—With increase in the size of the hydronephrosis, we first note a marked broadening of the entire

calix.   The terminal irregularities are to a great extent lost entirely
if the calix is fully distended.   Not infrequently with the disten-
tion of the calix there is an accompanying shortening.   This may
be present to such an extent that the site of the former calix is
designated by irregular indentation in the otherwise rounded
contour of the true pelvis.

Accompanying these marked changes in the outline of the calix
marked increase in size of the true pelvis may also be noted.   This
is seen distended with a smooth, well-rounded outline along its free
border which differentiates the mechanical from the inflammatory
distention.   This increase in size of the true pelvis may be out of
proportion to the changes in the calices.   With increase in size of
the true pelvis we also note a marked shortening of the papillæ
which normally project between the calices into the pelvis.   The
papillæ may become so flattened as to be practically effaced.

A point of interest in the diagnosis of hydronephrosis of a
limited or moderate degree is the change seen in the angle of inser-
tion of the ureter.   The course of the normal ureter as it leaves
the pelvis varies considerably, depending on the relative position
of the kidney and the first segment of the ureter.   With a low-
lying kidney, otherwise normal, the ureter may be seen to enter
the pelvis by a circuitous route.   However, when there is evident
acute angulation near the ureteropelvic juncture, with a distinct
increase in the size of the pelvis and definite changes in the outline
of the calices, the anomalous course of the ureter may be of corrob-
oratory value in demonstrating hydronephrosis.   An anomalous
insertion of the ureter without evidence of dilatation in the pelvis
could not, however, be regarded as the cause of any subjective
symptoms.

An element which may affect the general contour of the dilated
pelvis is that of secondary infection.   With interference of drain-
age from the kidney, secondary infection will frequently occur.
If the infectious process actively involves the entire kidney, it may
affect the general pelvic outline to a considerable extent.   The
entire pelvis will become irregular in outline and the calices appear
more accentuated and irregularly rounded.

Large Hydronephrosis.—The demonstration of a large hydrone-
phrosis by means of pyelography is, as a rule, unnecessary, since its
existence can usually be determined by the ordinary means of the
cystoscope and ureteral catheter. However, because of difficulties
in cystoscopic technic it may be occasionally necessary to make a
pyelogram in order to ascertain the exact condition present. The
comparatively small amount of colloidal silver solution injected
will usually be greatly diluted by the residual urine in the pelvis,
and the exact contour of the distention will not be demonstrated in
the pyelogram. A diffuse dim shadow extending over a wide area
usually indicates the extent of the pelvic distention. Not infre-
quently one or all of the calices appear as well-defined, irregularly
rounded areas scattered over the cortex, while the pelvic outline is
scarcely visible. This may be explained by the fact that the
injected fluid has remained undiluted at the ends of the partially
drained calices.

Differential Data.—In the course of a cystoscopic examination
data are frequently gained by means of the ureteral catheter which
may prove to be confusing and lead one to infer erroneously the
existence of hydronephrosis. The pyelogram is of value in differ-
entiating physiologic from pathologic conditions: (1) With con-
striction of the ureter, not permitting the ureteral catheter to
enter the pelvis; (2) with a short length of catheter and return
flow on overdistention; (3) with unusual length of catheter;
(4) hypersecretion.

It may be impossible to demonstrate the existence of hydrone-
phrosis in any other way than by means of the pyelogram when
the obstruction in the ureter does not permit the catheter to enter
the pelvis. It is self-evident that the amount of residual urine
could not be determined, nor would the overdistention method be
applicable. While but a small part of the fluid injected will pass
by the ureteral constriction into the pelvis, nevertheless enough
will usually enter to outline the existence of a hydronephrosis.

Not infrequently an unusually short length of catheter may pass
up into the ureter and, on injecting colored fluid, a rapid return
flow may be seen. This may frequently occur with the normal

low-lying kidney and may also be present with obstruction of the upper ureter. Further, folds of mucosa or a circuitous route of the ureter may prevent the catheter from being inserted to the fullest extent of the ureter. A fluid, such as colloidal silver, when injected into the ureter may pass such a physiologic obstruction when a catheter would not pass. The resulting pyeloureterogram demonstrates the actual condition at hand.

Occasionally in a flaccid ureter and pelvis a soft ureteral catheter may be introduced to an unusual length and lead one to infer that it is coiling up in a dilated pelvis. The position of the catheter as well as the exact size of the pelvis may be accurately determined by means of a pyelogram. Occasionally, because of reflex irritation or from other nervous stimuli, the rapidity of renal secretion may be so marked that the urine runs in a continuous stream with little or no peristaltic hesitation. As it drops rapidly from the catheter inserted in the renal pelvis one might easily infer that it is due to residual urine in a distended pelvis.

Etiologic Data.—A pyelogram is further of considerable value in demonstrating the etiologic factors present. It is of particular value in its power to demonstrate whether the obstruction is in the upper or lower ureter, whether primarily or secondarily inflammatory, whether due to change in the position of the kidney, and, lastly, not infrequently may point out the nature of the obstruction, particularly when subsequent to a constricting anomalous blood-vessel. While it is not of much practical value in determining clinically the actual cause of the constriction in the upper ureter, a contour of the hydronephrotic sac frequently has been noted peculiar to constriction caused by anomalous renal blood-vessels. The majority of anomalous blood-vessels which constrict the upper ureter enter the lower pole of the kidney, thus crossing the ureter several centimeters below the ureteropelvic juncture. In the subsequent dilatation the pelvis will dilate to a greater extent than the upper ureter. Consequently the general contour of the resulting sac will be pyriform. Of interest is the frequency with which an anomalous blood-vessel was found at operation to constrict the upper ureter and so cause the hydronephrosis. In a

paper written by W. J. Mayo, MacCarty, and the writer in 1909 it was noted that an anomalous blood-vessel was found at operation to be an etiologic factor in 20 out of 27 cases of hydronephrosis. Since then it has been found not quite so frequently, but in the 116 cases it was reported present in 71 (61 per cent.).

The more usual sources of error in the interpretation of the pyelogram are those due to: (1) Technical errors in pyelography; (2) difficulty of differentiation from the normal pelvis; (3) the indefinite shadows caused by dilution from retained fluid in large sacs; (4) incomplete distention of the pelvis and ureter.

Persistence of the Injected Medium.—In cases in which the results of the examination are unsatisfactory and the existence of a hydronephrosis is doubtful, evidence of the persistence of silver solution in the urine may be of value in the diagnosis. Under normal conditions all evidence of the silver solution in the urine should be absent in less than twenty-four hours after the injection. If the urine remains stained for several days, we have evidence of retention in some portion of the urinary tract. If a subsequent radiogram is taken twenty-four hours after the injection and the shadows of the retained injected solution are evident, the nature of the retention is apparent. This is apt to occur at the end of a calix which cannot be drained. Occasionally it will be seen as a diffuse, dim shadow made faint by dilution in the true pelvis.

Intrarenal Hydronephrosis.—The usual hydronephrosis is characterized by marked distention of the true pelvis, which is seen on surgical exploration of the kidney extending from the renal cleft as a distended, rounded sac. Occasionally, however, the distention is largely intrarenal, and in such cases, on section of the kidney, the calices will be found markedly distended, often extending to the very limits of the cortex, while the distention of the true pelvis is largely confined within the substance of the kidney. The parenchyma of the kidney is then considerably atrophied and limited in extent. It may be rather difficult to explain the intrarenal distention of the free pelvis. Frequently, however, it is due to peripye-

litis, with subsequent cicatricial tissue preventing the extrarenal distention.

Hematonephrosis.—A most interesting chapter in the study of hydronephrosis is the so-called bleeding hydronephrosis. While hematuria is not commonly found with hydronephrosis, occasionally it may be a prominent symptom. With the presence of marked hematuria the clinical data are frequently confusing. The clinical differentiation of a bleeding hydronephrosis from a renal neoplasm may be difficult. The hematuria is usually the result of a varicose condition of the pelvic mucosa, probably caused by chronic insidious infection. As a rule, such a hydronephrosis or hematonephrosis may be recognized by demonstrating the large amount of hemorrhagic residual urine in the pelvis. If a pyelogram is found necessary for identification, the outline of the hydronephrotic pelvis will readily be differentiated from the pelvic deformity accompanying other renal conditions which might cause hematuria. Hematuria with intermittent hydronephrosis was present in but 4 (3.4 per cent.) of the 115 cases.

Closed Hydronephrosis.—Not infrequently a patient may present himself because of abdominal tumor which may have appeared with little or no pain. The tumor may, on palpation, appear to be either cystic or firm, and may be so situated as to lead one to believe that it is a tumor of various extrarenal organs. All urinary symptoms may be absent and the urine normal. If the tumor is caused by a closed hydronephrosis, the cystoscopic examination alone will reveal the true state of affairs. No secretion of urine will be noted from one meatus, while the secretion from the other will be unusually large in amount. The catheter will meet with impassable obstruction at a variable distance up the ureter. The type of hydronephrosis which goes on to complete closure occurs usually without pain. The occlusion is, as a rule, probably sudden, with the kidney in a previously normal condition. Closed hydronephrosis is frequently unrecognized prior to operation, and is more commonly mistaken clinically for cystic gall-bladder and ovarian or mesenteric cyst. Every doubtful tumor, particularly in the upper lateral abdomen, should have the possibility of renal

involvement excluded, even though the urinary data are negative.

Postoperative Course.—Of considerable interest is the course of the hydronephrotic sac following the removal of the ureteral obstruction at operation. If the dilatation has not been too great, and if there is no marked degree of secondary infection, the sac may resume practically its normal contour in the course of time. This is well illustrated in a pyelogram which was taken three years after a plastic operation for hydronephrosis. At the time of operation a hydronephrosis of three or four ounces was found. Three years later the hydronephrosis showed in the pelvis practically normal in outline, with a capacity of 28 c.c. In another radiogram recently made we had an example, on the other hand, of the plastic operation performed five years before on a hydronephrosis of approximately four ounces capacity, and which at the present time is still dilated. The absence of objective symptoms and the character of the secretion on that side, however, show that considerable functional capacity still remains in the kidney. The pelvis remains enlarged to a variable degree in the majority of cases of well-marked hydronephrosis following plastic operation.

In this series of 116 cases of hydronephrosis nephrectomy was done in 84 (72 per cent.) cases; a plastic operation on the pelvis in 15 (13 per cent.) cases; and division of the ureter and nephrorrhaphy in 17 (15 per cent.). Plastic operation on a large hydronephrosis of a capacity of more than five or six ounces is usually not successful. In practically every case where nephrectomy was necessary there had been unrecognized symptoms of long duration. Had these cases been diagnosed early, even within two or three years after the beginning of the first symptoms, a plastic operation might have sufficed to restore function. The early diagnosis of hydronephrosis is greatly to be desired.

THE SMALL KIDNEY, WITH SPECIAL REFER-
ENCE TO THE NEW FORMATION OF
TUBULES *

ELLERY D. SIMPSON

My object in presenting this paper is: (1) To report more or less in detail the pathologic conditions found in the kidneys of a child thirteen months old, one of the kidneys being of the infantile contracted type; (2) to give a brief general description of

<div align="center">A   B   C</div>
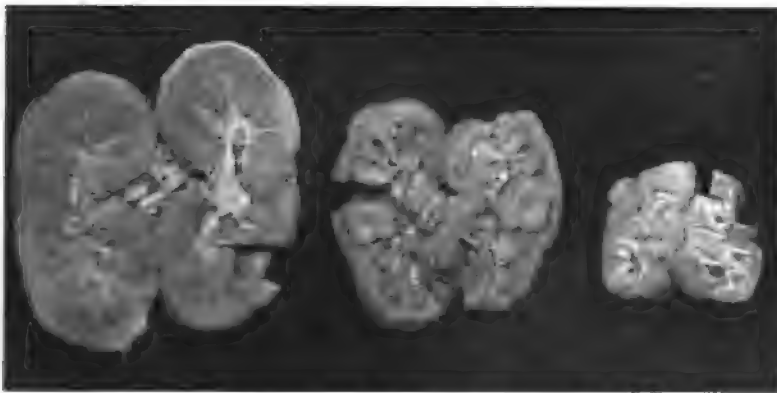
Fig. 118.—(64475.) Kidneys from girl aged thirteen months, natural size. A, Compensatory hypertrophy of kidney on left side, Case 64475, 56 grams. B, Normal kidney of child, Case 26231, thirteen months, for comparison. C, Infantile contracted kidney from right side (64475), weight, 9.6 grams.

our present knowledge concerning the small kidney; and (3) to review certain observations relating to the formation of new tubules in the contracted kidney.

The material studied consisted of undersized kidneys ranging in weight from 9.6 grams to 121 grams. These were removed either at operation or autopsy at the Mayo Clinic from January 1, 1905, to January 1, 1914.

For convenience of study small kidneys may be classified into the following types:
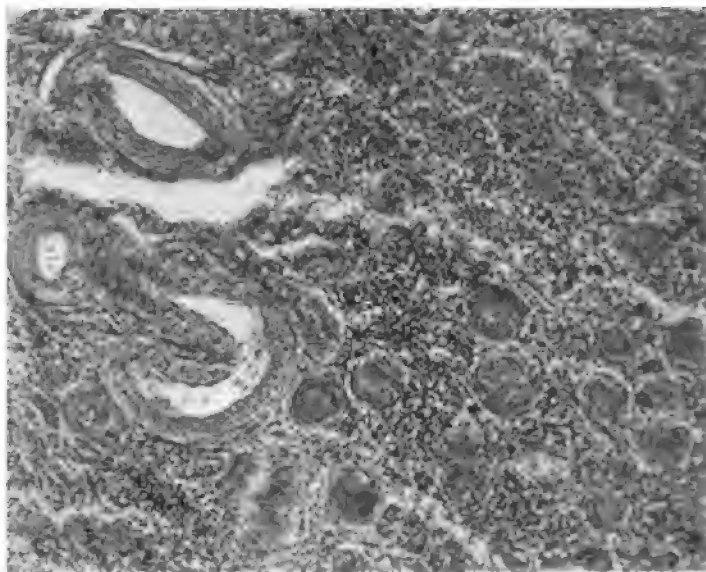
Fig. 119.—(64475.) Chronic interstitial nephritis (infantile contracted kidney). Microscopic section of kidney shown in Fig. 118, C. Almost every glomerulus shows hyalinization. Glomeruli very close together. Increase of interstitial connective tissue. Pronounced thickening and hypertrophy of walls of blood-vessels.

I. Infantile.

  Arrested or defective development, with or without pathologic involvement.

II. Contracted kidney.

  (a) "Genuine" or "primarily contracted kidney."

  (b) Atherosclerotic kidney (patchy sclerosis of Ziegler[1]).

  (c) Secondary contracted kidney (chronic interstitial nephritis).

(*d*) Hydronephrotic contracted kidney (Aschoff[2]).

(*e*) Senile kidney.

III.   Amyloid degeneration (syphilis and tuberculosis).

REPORT OF A CASE OF INFANTILE CONTRACTED KIDNEY

CASE 64475.—D., female, aged thirteen months.

Family history negative. *Previous diseases:* Severe attack of lobar pneumonia when one and one-half months of age. *Present illness:* Duration, thirty-one hours; characterized by vomiting and restlessness. *Operation:* Emergency, February 21, 1912. *Findings:* Intussusception at ileocecal coil of ileum into cecum, transverse and ascending colon. Appendix black from reduced circulation. *Procedure:* Intussusception reduced and appendectomy performed (acute catarrhal appendicitis). Patient died on the sixth day. *Autopsy report:* Intestinal obstruction due to adhesions (foot above ileocecal valve). Early general peritonitis. Congenital very small right kidney; hypertrophied left kidney.

Examination of the Kidneys

Smaller Kidney (Right)   (Fig. 118, C)—*Macroscopic Examination.*—Specimen preserved in 10 per cent. formalin. Weight, 9.6 grams. Size, 3.7 x 2 x 1.3 cm. The capsule was not apparently thickened and was slightly adherent in places. The surface was smooth, and the lobulation, for the most part, had disappeared. It was not uniform in size, but presented two prominences of a pale yellow color and standing out in marked contrast to the surrounding grayish-white depression. The larger of these prominences was at the lower pole, anterior surface, and measured 1.6 x 2 cm., presenting an elevation of from 3 to 4 mm. The smaller prominence measured 1 x 0.9 cm. and bulged perceptibly. It was located at the upper pole, convex surface, and posteriorly. The kidney cut with somewhat increased resistance. The cortex at the prominences was 7 and 3 mm. in width respectively. The cortex here was distinctly marked, while elsewhere it was thin and indistinct, being about 1 millimeter in width. The small blood-vessels penetrating the substance of the kidney were gaping and stood out prominently. Some of the pyramids were obliterated, and the remainder were short, 3 to 5 mm. in length, were narrow and very pale, with indistinct markings. The pelvis encroached upon the cortex, was thickened, and appeared somewhat dilated. It contained a small amount of fat.

Microscopic Examination.—The pale yellow prominences were composed of renal tissue that, save for the very slight grade of acute nephritis, was nearly normal. The glomeruli and tubules showed no maldevelopment. The histologic picture was very similar to that of the larger kidney, the glomeruli being larger and further apart than is normal for a kidney of thirteen months. The tubular epithelium was somewhat increased. In other words, these elevations represent areas of local compensatory hypertrophy.

The remaining portion of this kidney presented a picture in every way different from that just described. The most striking feature was the very marked increase of interstitial connective tissue (90 to 95 per cent.) (Fig. 119). There was a marked diffuse, small, round-cell infiltration, more pronounced in the cortex. Almost every glomerulus was completely obliterated by hyalinization (98 per cent.); the few remaining glomeruli showed this to a less extent, and the latter were surrounded by an increased amount of elastic tissue. The glomeruli were very close together, 20 in one low-power field as compared with 7 in such a field in the previously mentioned elevated areas. There was a marked disappearance of tubules (95 per cent.), those remaining either being dilated with markedly flattened cells, or without any cells at all, or collapsed. A few were filled with hyaline casts. The pronounced thickening and hypertrophy of the muscularis (tunica media) was the most marked feature of the type of sclerosis of the arterioles and arteries and probably represented the earlier conditions of sclerosis. Another characteristic feature was the surrounding fibrosis or so-called chronic peri-arteritis. The wall of the vessel was about twice as thick as normal, or about the thickness of that in an adult arteriosclerotic contracted kidney. This change in the wall of the vessel does not occur in the more normal renal tissue.

The arteriosclerosis in this case probably resulted from primary injury to the glomeruli, which in turn caused increased tension of the arterioles and arteries. The alteration of the blood-supply must have been slow because of the great development of cicatricial tissue and the marked contraction and atrophy. This organ may be rightly called an infantile contracted kidney from unilateral chronic interstitial nephritis.

Larger Kidney (Left) (Fig. 118, A)—*Macroscopic Examination.* —Specimen preserved in 10 per cent. formalin. This kidney presented a picture of a true compensatory hypertrophy. It weighed 56 grams, the combined weight of two normal kidneys of

this age. Its size was 7.7 x 3.7 x 3.8 cm. The capsule was normal and stripped easily. The surface was normal in appearance, smooth, and presented typical deep lobulations (fetal). Resistance to the knife was normal. The cortex was wider than is normal for a kidney of this age, and measured 5 mm. (13 mm. at the tips), the markings being everywhere distinct. The pyramids were enlarged, otherwise normal. They were distinct and measured 10 to 15 mm. in length. The pelvis was normal.
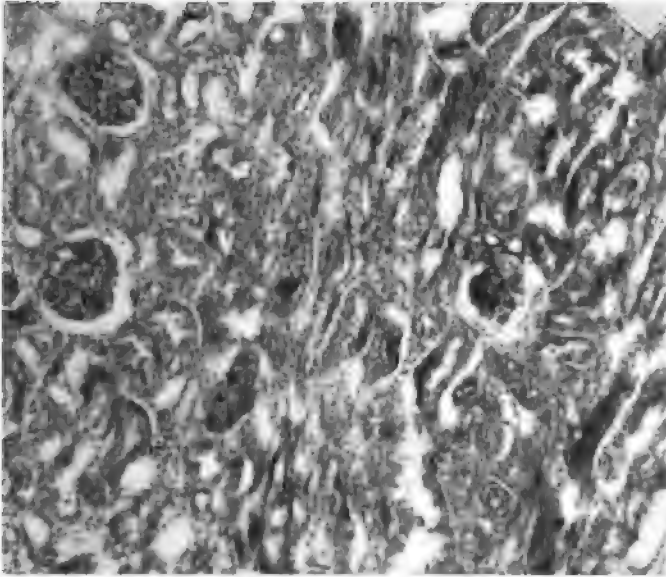
Fig. 120.—(64475.) Compensatory hypertrophy or hyperplasia of renal parenchyma. Section from kidney shown in Fig. 118, A. Normal renal tissue save for slight degree of acute nephritis. Enlarged glomeruli and increase in tubular epithelium.

Microscopic Examination.—The histologic picture was that of a compensatory hypertrophy or hyperplasia (Fig. 120). There was a regenerative increased growth of the renal parenchyma. The substance was normal save for the very slight degree of acute nephritis. The glomeruli were about one-third larger than is normal for such kidneys. The glomeruli averaged seven in a low-power field, or the same number as for such an area in the kidney of a child seven years old. There was an increase in the tubular epithelium. The vessel-walls were of normal thickness. Such a

kidney is especially liable to disease, inasmuch as its reserve power is small.

The smaller kidney was found to be about the size and weight of a normal kidney of a full-born child eight weeks old. In such a kidney the cortex markings and pyramids are very distinct, the cortex measuring about 2 mm. (4 mm. at the tips) and the pyramids 8 to 12 mm. in length. The larger kidney was about the size and weight of a normal kidney of a child seven years old. In such a kidney the cortex measures about 5 mm. (12 mm. at the tips), and the pyramids are about 10 to 13 mm. in length.
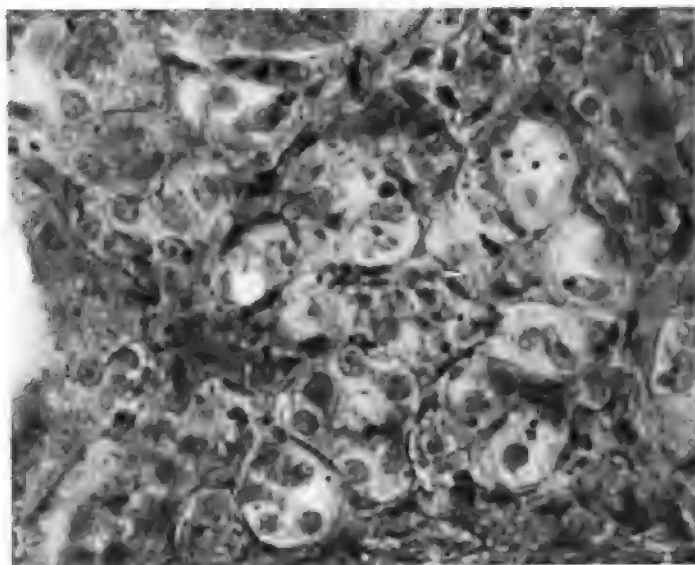
Fig. 121.—(5939-Pl.) Arteriosclerotic contracted kidney. Field immediately beneath capsule of kidney filled entirely with buds, each containing two to five cells in transverse section.

The normal kidney of a child twelve or thirteen months of age should weigh about 28 grams. The size should approximate 6.3 x 3.3 x 2.8 cm. The capsule should come off easily. The surface should be smooth, uniform, and present (fetal) lobulations. The cortex measures 4 mm. (10 mm. at the tips). The pyramids are 8 to 12 mm. in length (Fig. 118, B).

The normal fresh adult kidney, according to Piersol,[2] weighs

about 130 grams (4½ ounces), slightly less in the female, and measures about 11.5 cm. (4½ inches) in length, 6 cm. (2½ inches) in width, and 3.5 cm. (1½ inches) in thickness. The left kidney is usually somewhat longer, narrower, thicker, and slightly heavier than the right.

The question naturally arises, is there any difference between the microscopic picture of chronic interstitial nephritis in the infantile contracted kidney and that in the "genuine contracted kidney," which occurs in the adult? After careful comparison, I have been unable to detect any dissimilarity save possibly the fact that some of the hyalinized glomeruli may be slightly undersized as compared with such glomeruli in the adult diseased kidney. The interstitial connective tissue may be not quite so dense. Even the walls of the blood-vessels are of the same thickness as in the adult arteriosclerotic kidney. This striking similarity may be accounted for by the fact that the tissues in the young are more elastic, so to speak, than in the adult. Hence the rapid and great increase of interstitial connective tissue in such a short time as compared with the longer time consumed in bringing about such a change in the previously healthy adult kidney. For this same reason we can understand why, as in the above reported case, the hypertrophied kidney is approximately the same weight as that of two normal kidneys in a child of the same age. Should one kidney become diseased in an adult, the other very rarely becomes hypertrophied to such degree as to be equal in weight to both kidneys before any pathologic change occurs.

According to Adami,[4] congenital hyperplasia of one kidney (infantile kidney) is not rare. It arises either through intrinsic causes inherent in the germ and, therefore, inheritable, or through the action of extrinsic injurious influences upon the normal anlage during the course of development. The gross and microscopic pictures are both normal. It differs from the normal kidney in its diminutive size only. Such a kidney may early be subject to disease, as in the case I have just reported.

Chronic interstitial nephritis in children, according to Heubner,[5] while relatively rare, has been seen by many observers. It

is believed to be hereditary in some cases, but most cases are probably, as Heubner suggests, due to previous infections, *i. e.*, scarlatina, measles, pneumonia, interstitial disturbances due to bacteria, etc. According to Herrick,[6] chronic interstitial nephritis, whether in adults or children, is almost always bilateral. Unilateral chronic interstitial nephritis, he says, is extremely rare. Guiteras,[7] he continues, in 500 autopsies on patients with chronic Bright's disease, did not note an instance in which one kidney alone was involved, nor was a single instance of unilateral nephritis ever seen by Kümmell[8] in the rich autopsy material at Hamburg. Among renal diseases certain forms of infantile contracted kidney are of syphilitic origin, but in this realm little is definitely known.

Barker[9] has lately reviewed recent studies concerning the different forms of "contracted kidney" as carried on by leading pathologists in this country and in Europe. The contracted kidney is a result of various earlier processes which may be very different from one another. The "genuine contracted kidneys" make up the greatest number of small kidneys, and occur in individuals who are affected with a general arteriosclerosis. The atherosclerosis of the small kidney arterioles causes decreased supply of blood to many glomeruli, thereby bringing about hyaline degeneration and atrophy of the corresponding tubules.

Another form of atherosclerotic kidney is characterized by atrophy in patches and is caused by involvement of single branches of arteries supplying the kidney. This type is known as the "atherosclerotic kidney" of Ziegler.

According to Aschoff, every now and then a healing interstitial nephritis or a preceding embolic nephritis leads to contracted kidney. Recent works have shown that only very rarely does a glomerular nephritis lead to contracted kidney. Chronic cases may have their histologic pictures complicated by various processes of regeneration and hypertrophy, thereby making the interpretation of a given end stage extremely difficult.

The frequency in general of kidneys atrophic through various causes is seen from a study of 3940 necropsies from the pathologic department of the Johns Hopkins Hospital.[10] Among this

number, 36 cases of atrophy from various causes were found. Of these, only 6 were unilateral, and of the 6, 3 belonged to the infantile type seen in adults. This tabulation naturally does not include the moderate bilateral diminution in size found in some cases as a result of chronic nephritis.

It has been shown experimentally that the removal of three-fourths of the renal substance results in death from emaciation and asthenia in from one to six weeks (Bradford[11]). The factor of safety is two-thirds, and the indispensable amount of renal substance required by the animal not over one-third (Meltzer[12]). Such a reduction may be considered analogous to advanced atrophy of the kidney in man. It has been determined that a man after the entire removal of both kidneys will live from ten days to two weeks.

New Formation of Renal Tubules.—The epithelium of the kidney is capable of proliferation, and small losses in the tubular epithelium are quickly replaced. When one kidney is removed or remains small because of arrested development, compensatory hypertrophy of the other organ sets in, its beginning being indicated as early as the third day by the presence of karyokinetic figures. It is now accepted that epithelial cells originate only from epithelial cells. It is only when preëxisting epithelial cells multiply that we get regeneration of epithelium. Pathologic new-growths of epithelial cells always spring from epithelium. Regeneration of epithelium occurs also in the thyroid and liver. It is a general rule that the different types of epithelial cells are not interchangeable, *i. e.*, flat epithelium produces only flat epithelium, etc.

Stoerk,[13] in a comparatively recent article concerning the Grawitzian tumors, describes histologically, as a side issue, two methods of new formation of renal parenchyma: (1) Elongation and winding around of the existing canaliculi, and (2) ramifications due to new buddings. He states also that it is in the little pale protuberances which are to be found on the surfaces of certain granular contracted kidneys that the most active ·formation of renal parenchyma occurs. It is with these two pictures in

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mind that I have studied the series of small kidneys herein reported.

As concerns these processes of new formation of renal epithelium, I have seen tubules that had become lengthened and which lengthening was either straight or through complex windings. This is brought about by an increase in the number of epithelial cells. Mitotic figures are present. The epithelial cells of the con-
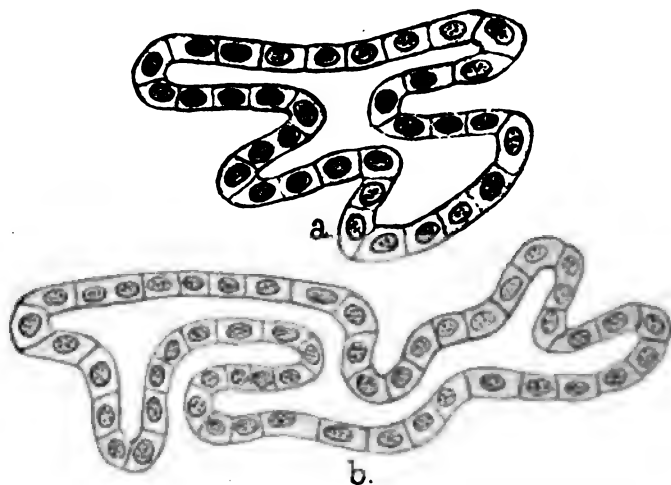
Fig. 122.—Elongation and winding around of renal tubules. *a*, Winding around of renal tubule; *b*, elongation and winding around renal tubule.

tracted tubules are of regular contour and are slightly lower in height as compared with surrounding tubules (Fig. 122).

It is with the new bud formations that I wish especially to deal. In this series these canalicular outgrowths occurred in the atrophic and arteriosclerotic kidneys. The buds may occur either in the small elevated white bodies which are on the surface of the kidney or in the depressions. They may occur in single groups or be isolated between the cortical tubules. They usually

occupy atrophic regions of the cortex, either between the tubules
or around sclerosed glomeruli.   In my sections the only location
where I found fields filled entirely with buds was immediately
underneath the capsule.   Such fields were almost invariably in
depressed areas and very close to hyalinized glomeruli.   The buds
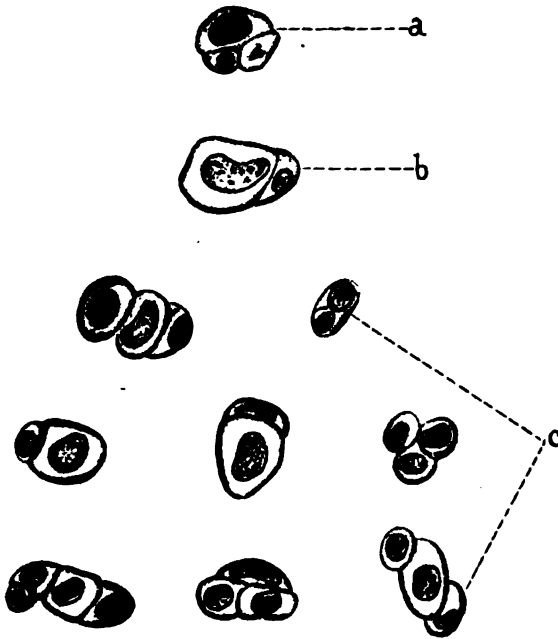
Fig. 123.—New bud-formations from renal canaliculi: *a*, Beginning lumen formation.   Mitotic figure in lower right cell; *b*, characteristic faint pink, almost unstaining, cell protoplasm; chromatin of nuclei equal in distribution; no clumping of chromatin, *c*, almost unstaining cell protoplasm. Each bud contains from two to four cells.   Chromatin mainly at periphery of nuclei; no clumping of chromatin.

in these fields are close together, with nothing intervening.   Such
a location seems natural, for should a glomerulus be normal in
structure, its tubules would not be destroyed, and there would be
no need of new formation of tubules around it.

Tubule proliferation in atrophic nephritis occurs in multiple

and widely distributed foci. Such areas usually contain small
round-cell infiltration. These newly formed tubules are usually
lumenless and inclose two to five cells (transverse section)
(Fig. 121). They may, however, contain lumina. The proto-
plasm of the cells is abundant, but almost unstaining (Fig. 123).
The cells are of unequal sizes. The nuclei are round or slightly
oval, and are pale. The chromatin, according to Stoerk, stains
mostly at the periphery, although in my specimens the chromatin
sometimes appears homogeneous. One may come across mitoses
in the buds. These buds can be distinguished from atrophic
canaliculi. The latter are characterized by dark staining, granular
protoplasm (scanty dark protoplasm). The cells are often de-
formed, and there is clumping of the chromatin of the nuclei. The
buds may also be differentiated from similar structures occurring
in neoplasms (hypernephromas). In such growths, as pointed out
by Stoerk, there are from 20 to 30 cells in a group instead of from
two to five. Further, the cells are swollen, irregular, very poly-
gonal, and flattened together. Nearly every single cell-complex is
surrounded by a capillary. There is a fine band of tissue between
the single cell-complexes.

These new formations, as pointed out by Stoerk, seem to arise
from proliferation of the adult secreting epithelium of the con-
voluted tubules. I have in a few instances seen portions of certain
fields under the microscope which showed a characteristic sprout-
ing of cells from the preëxisting tubules. Such sprouts were
composed of solid cells which were not as yet grouped to form a
lumen. Apparently they do not arise from the islands of nephro-
genic tissue (primitive renal blastema) which is sometimes present
in the adult kidney.

As to the outcome of the buds, probably most of them are
destroyed and disappear. This is natural because of the more
rapid and greater increase of connective tissue, and the conse-
quent blocking of the blood-vessels. Those that remain cannot
functionate because they cannot come in direct contact with the
glomeruli.

It is well known that the higher and more specialized the

tissue, the less its capacity for regeneration. Of all the tissues, the ordinary connective tissue has the greatest proliferative capacity, and in the process of healing we observe that this overwhelms the other regenerating tissues. The tendency on the part of the newly formed connective tissue to contract, thus inducing atrophy of the cells, is the main hindrance to adequate regeneration.

As regards the so-called "hypernephroma," the character of the cells in a large proportion of the tissues of such growths is, as Stoerk has shown, quite analogous to structures in regenerating renal tubules. Stoerk even goes so far as to say that "hypernephromas" arise from proliferation of the adult secreting epithelium of the convoluted tubules.

It is not my purpose to discuss the extensive subject of "hypernephroma"; suffice to say that it has been shown by Wilson,[14] in a paper dealing with the study of the histology of 48 "hypernephromas," and in which he also refers to Stoerk's two processes of new formation of renal tubules, that such neoplasms do arise from islands of nephrogenic tissue (primitive renal blastema).

The above findings concerning the new formation of tubules in the kidney, which are in nearly every way identical with those observations made by Stoerk, comprise the study of 81 undersized kidneys in individuals whose ages range from thirteen months to seventy-one years. The weights of the kidneys are anywhere from 9.6 grams to 126 grams. Buds were found in 25 of the kidneys; elongation and widening of tubules in 18, while in 5 cases both elongation and widening of tubules and new bud formations existed in the same kidney. In all instances in which the above findings were positive the connective-tissue increase ranged anywhere from 10 to 95 per cent. The percentage of hyalinized glomeruli ranged from 10 to 100. In 5 of the 81 cases fairly large-sized fields of pure buds were observed, while in the other cases the buds were few, more or less isolated, and widely separated.

CONCLUSIONS

1. Unilateral chronic interstitial nephritis (infantile contracted kidney), though extremely rare, does occur in children one year of age.

2. The "genuine contracted kidneys" make up the greatest number of small kidneys, and occur in individuals affected with a general arteriosclerosis.

3. On my observations on the histologic study of "contracted kidneys," I venture to extend Stoerk's suggestion that there are two methods of new formation of tubules in such kidneys: First, elongation and winding around of tubules; and second, ramifications due to new buddings.

4. As pointed out by Stoerk, these new formations appear to arise from proliferations of the adult secreting epithelium of the convoluted tubules.

5. Both methods of new formation of renal tubules occur in individuals whose ages range from thirteen months to seventy-one years, the undersized kidneys in said individuals ranging from 9.6 grams to 126 grams, and in which kidneys the percentage increase of interstitial connective tissue is anywhere from 10 to 95 per cent., and the percentage of hyalinized glomeruli from 10 to 100.

6. The regeneration in the kidney in the sense of new formation of tubules is important and interesting in that it shows the attempt on the part of nature to replace lost secreting structures.

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RENAL CANCER ASSOCIATED WITH RENAL STONE *

JOHN R. CORYELL

The object of this paper is not to advance a new theory nor to discredit an old one, but to record the macroscopic and microscopic findings in kidneys the seat of both stone and cancer.

The method of procedure has been as follows:

1. Review of the primary pathologic diagnosis which was made on frozen sections stained with Unna's polychrome methylene-blue in the diagnostic laboratory immediately after removal of the organ.

2. Study of the gross specimen.

3. Microscopic examination of sections from cortex, medulla, and pelvis of specimens kept in 10 per cent. formalin, frozen and stained with hematoxylin and eosin; also of serial paraffin sections of many specimens stained with Sudan III and Scharlach R, and with Weigert and Van Gieson.

The study covers all cases of renal cancer and renal stone from which tissue was removed in the Mayo Clinic from January 1, 1905, to July 1, 1914, a total of 145 cases, of which 131 were of stone only, 5 were cancer only, and 9 were cancer associated with stone.

CHRONIC IRRITATION FROM RENAL STONE

A great deal has been written on the relation between chronic irritation and the formation of cancer. That the two processes are frequently associated cannot be questioned. Whether cancer is the direct result of chronic irritation or whether the latter plays the part of an extraneous exciting agent and determines the locali-

zation of the former in an organism which contains some sort of a chemical sensitizing substance (Loeb), or is influenced by some hereditary factor (Slye), is still an open question.

The expression, chronic irritation, is very broad in its scope, and includes, under a single term, mechanical agents, as trauma, pressure (continuous or repeated), friction, shock, dust, smoke, and foreign bodies of every kind as well as organisms living or dead; chemical agents, notably those concerned in the so-called occupational cancers of dye- and paraffin-workers and of chimney-sweeps; and physical agents, as heat, x-rays, light, electricity.

In 1823 Breschet and Ferrus stated their opinion that cancer invariably succeeded irritation or inflammation, and was incapable of being developed except in places where either of those states had preëxisted (Walshe).

Virchow, in the early sixties of the last century, sought to explain the inception and development of cancer by irritation starting the cells upon a career of lawless growth. To-day Virchow's theory is accepted by many investigators as an explanation—to a certain degree—of the etiology of malignant proliferation.

Trauma, as a form of irritation, has been observed by Coley, who in 1911 reported personal observations on 250 cases of carcinoma in which there was a history of trauma in 32.8 per cent. He refers to the work of Röpke who, in 1905, in a study of the material at the Surgical Clinic of Jena, collected statistics of 800 carcinomas "plus a larger number of cancers associated with chronic irritation," showing that in carcinoma chronic irritation seems to play the more important rôle. Ziegler states that, of 170 cases of carcinoma, 37 cases, or 22 per cent., gave a history of a single antecedent trauma; Estlander gives 59 cases with 15 antecedent traumas (25.4 per cent.); Snow, 22 per cent. in 143 cases; Henry, 16.8 per cent. in 196 cases—all preceded by a single trauma.

Levin, in 1910, gave a table of 2882 cases of cancer involving different parts of the body. In 545, or 19.2 per cent., there was a definite history of previous local reaction.

The following are the principal reported examples of cancer developing at the site of irritation of varying duration and intensity:

Cancer of the uterus in women who have borne children, more common than in virgins.

Cancer of the cheek associated with the eating of very hot rice in certain provinces of China.

Cancer of the abdomen subsequent to burns from the Kangri or charcoal stove worn by the people of Kashmir.

Epithelioma of the mucous membrane of the mouth associated with chewing betel-nut mixed with lime—which is very irritating —by Hindus.

Cancer of the penis developing on a chronic balanitis or unrelieved phimosis.

Gastric cancer developing on gastric ulcer (Wilson and Mac-Carty). "Hauser was the first to show that in gastric ulcer new tubular glands are formed which are lined by cylindric cells and may undergo cystic dilatation; and to call attention to the development of gastric cancer on a gastric ulcer" (Wilson). The most recent compilation of statistics from operative material shows that approximately 57.4 per cent. of the gastric carcinomas develop on a gastric ulcer (Wilson and McDowell). Moynihan gives 60 per cent.; Mayo Robson, 59 per cent.

In an examination of 5000 appendices in the Mayo Clinic, 22 were found to have developed cancer. "Obliteration of lumen occurred in 22.8 per cent., and 90 per cent. of the carcinomas occurred in partially or completely obliterated appendices. All were associated with chronic inflammation" (MacCarty and McGrath).

Of 27 colons with diverticulitis, 11 had cancer ingrafted on them (Telling, quoted by Giffin and Wilson).

Cancer of gall-bladders previously affected with gall-stones. "In nearly all of the cases of our own series, gall-stones were present" (Mayo).

Cancer of the lip in smokers.

Tumors of the bladder, benign and malignant, in anilin dye-workers.

Cancer among x-ray workers.

Cancer of the breast after chronic mastitis.

Epithelioma after lupus or tuberculosis of the skin (L. Sava-tard).

Sarcomatoid hyperplasia of lymph-nodes in tuberculosis.

Hypernephromas preceded by renal calculi (Ewing).

Cancer of scrotum in chimney-sweeps and in paraffin workers.

Epitheliomas of the eyelids. Fisher reports that of 88 cases, 46 per cent. were in the lower lid, and 36 per cent. at the inner canthus; "these parts are usually hyperemic when the upper lid and outer canthus show comparatively little evidence of irritation." They are more frequently irritated by tears and foreign matter.

Rodent ulcer succeeding a hard pimple near the angle of the eye (Hutchinson).

Cancer on the margin of the lower lip, developing from a "crust."

Cancer from warts, cutaneous horns, sebaceous cysts, papillomas, and ulcers (simple or specific) of the skin.

Cancer of the skin developing in tar, carbon, and asphalt workers.

Prostatic cancer beginning where a chronic prostatitis is present (Young).

Local trauma of any kind (Coley).

Epitheliomas developing at the base of the right horn of cattle used to haul carts by a rope fastened to the right horn.

Cancer in horses where the bit irritates the corners of the mouth (Plicque).

Subcutaneous fibromas under the collar and girth of horses (Plicque).

Carcinoma of the posterior mammæ of dogs, the ones most frequently congested (Plicque).

Cancer of the upper lip of cats, the one more likely to be wounded.

Papillary epitheliomas on the tongues of rats fed for a long time on cats (Stahr).

Ribbert obtained small but typical papillary growths on the inner surface of the rabbit's lip by repeatedly scraping certain parts, again denuding them as soon as the epithelium was regenerated, and finally allowing them to heal.

Clunct produced sarcoma in the rat by repeatedly exposing it to x-rays.

Rous has shown that more rapidly growing tumors developed at the site of trauma than elsewhere in the body.

Kelley refers to papillomas developing on sheep's noses from grazing upon short stubble.

Perhaps the first to call attention to the precancerous condition of the cell was Hutchinson, who spoke of it fifty years ago (Wood). Ribbert, in 1901, emphasized the importance of this stage of the cell.

Levin succeeded in increasing the susceptibility of rats to sarcoma by previous local irritation from injections of scarlet red and ether; and established "the first experimental proof of the existence of a local 'precancerous stage.'"

In kidneys the seat of stones one of the earliest changes is a proliferation of fibroblasts beneath the tubular epithelium. The new tissue thus produced apparently upsets the balance between the epithelium and the connective tissue, which is followed by a proliferation of the epithelium. Here, at least, the epithelial multiplication seems to be due to a chronic irritation, set up by the stone. Thiersch accepts the pathologic condition in the connective tissue by which the connective tissue becomes less resistant against the epithelial cells. "The epithelial growth follows the analogy of normal gland formation, while, owing to a process of adaptation to the abnormal environment and loss of function the atypical structure of cancer results" (Ewing). Ewing refers to Hansemann, who uses the term "anaplasia" in conditions of tumor—cell changes which show unequal, asymmetric, and multipolar mitoses and destruction of chromosomes of frequent occurrence, particularly in the more malignant tumors. More or less anaplastic cells occur

in inflammatory processes—cells with irregular mitosis. This strengthens the theory of the relationship between chronic irritation and tumor formation. Further, gametoid mitosis has been brought about in plants by means of chemical irritants, which would seem to add even more evidence to this theory.

In some of the sections of kidneys from cases of renal stone associated with renal cancer there seems to be a tendency on the part of the cancer-cells to mimic the renal tubules. In places the
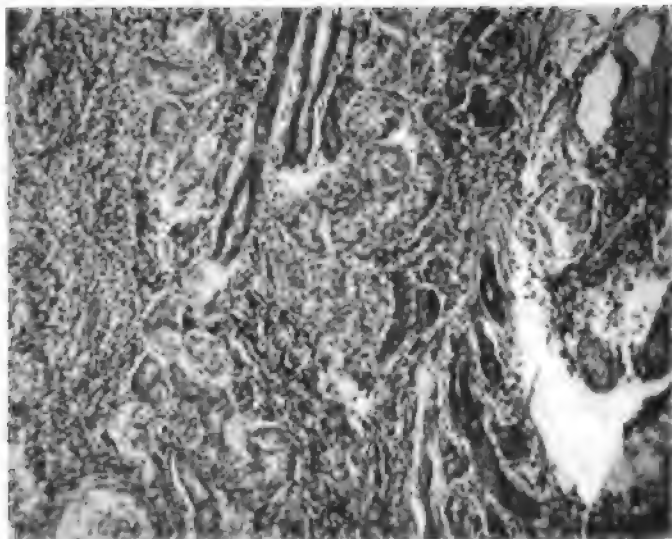
Fig. 124.—(A2662) 120D. mag. Showing attempt of cancer-cells to mimic renal tubules in their
arrangement.

epithelial cells, supported by a delicate framework of connective tissue, are arranged in columns, the central cells of which have apparently undergone degeneration and absorption, thus giving an appearance somewhat similar to that of renal tubules. The tubules are obviously of neoplastic origin; the component cells are distinctly cancerous, and the general and minute appearance is different from that of regenerating tubules (Fig. 124). In this case the cancer was limited to and derived from the renal pelvis.

In several sections of kidneys containing stones are seen regen-

erating tubules.   Their appearance, with both the low and the
high power, is embryonic.   The newly formed or regenerating
tubules are often surrounded by a small amount of delicate strands
of connective tissue supporting capillaries, and at times slightly
infiltrated with lymphoid cells.   These tubules are somewhat nar-
rower than the mature ones.   The lining cells are proportionately
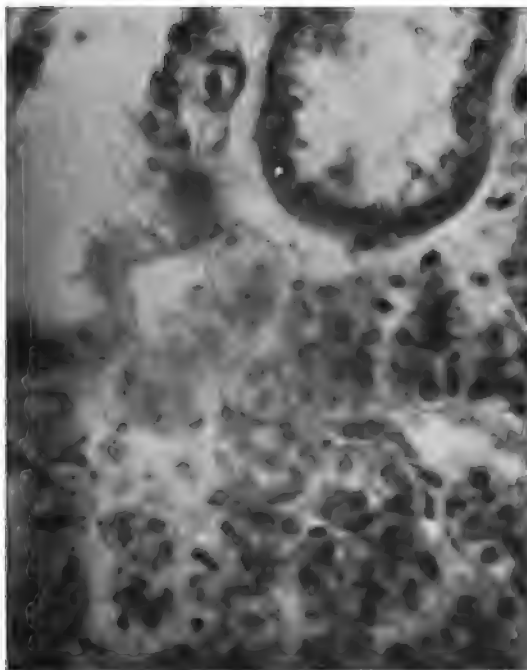
Fig. 125.—(A91687.)   250 D. mag. of regenerating renal tubules, showing embryonic character
of the cells.   Large, deeply-stained nuclei in lower right corner.   Above are old tubules, cut longi-
tudinally, showing disintegrating cells.

larger than the epithelial lining of fully developed tubules.   The
nucleus is large and stains readily with hematoxylin, and at times
nucleoli may be seen.   The nuclear and cell-membranes are dis-
tinct.   Some cells contain two nuclei, but no chromosomes or early
mitotic figures are seen (Fig. 125).

In kidneys the seat of stone and cancer, where the cancer is not
actually invading the substance of the gland, but where it is sepa-

rated more or less completely by bands of connective tissue or by blood-vessels (Figs. 126 and 127), the preparatory inflammatory changes, *i. e.*, the formation of fibroblasts, new capillaries, and lymphoid infiltration—which is often marked—seems to be entirely apart from the neoplasm.   In other areas, where the inflammatory changes seem to be absent or of a lesser degree, cells which are with great difficulty distinguished from neoplastic cells are present in varying numbers interspersed among the connective-tissue cells.
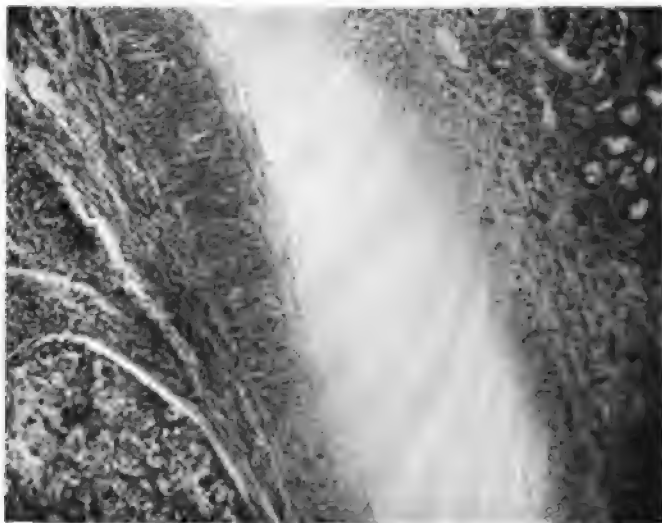
Fig. 126.—(A49100.)   50 D. mag. showing renal substance (glomerulæ and tubules) with a large artery separating it from a cancerous area.

Whether these are embryonic connective-tissue cells or precursors of cancer-cells it is almost, if not quite, impossible to decide. "Inflammatory hyperplasia passes by insensible gradations into a neoplastic growth" (Ewing).   In places, at the periphery of the cancer, there is a network of fine connective tissue and in some places there are engorged capillaries.   In the meshwork of connective tissue, as a rule, lymphoid cells predominate, but in many places there are cells which, although probably inflammatory in character, are with difficulty assigned to the group of neoplastic

cells or to that of inflammatory ones.   Their protoplasm stains
with varying degrees of intensity with eosin; at times it is finely
granular, at others it is clear and sometimes vacuolated.   The
nucleus usually stains deeply with hematoxylin, showing a well-
defined border and a nucleolus.   The cell outline is usually dis-
tinct.   The shape of the cell is frequently modified by pressure—
one often sees round, polygonal, fusiform, and even flattened cells.
When pressure is absent, the cell is usually round.   In size the cells
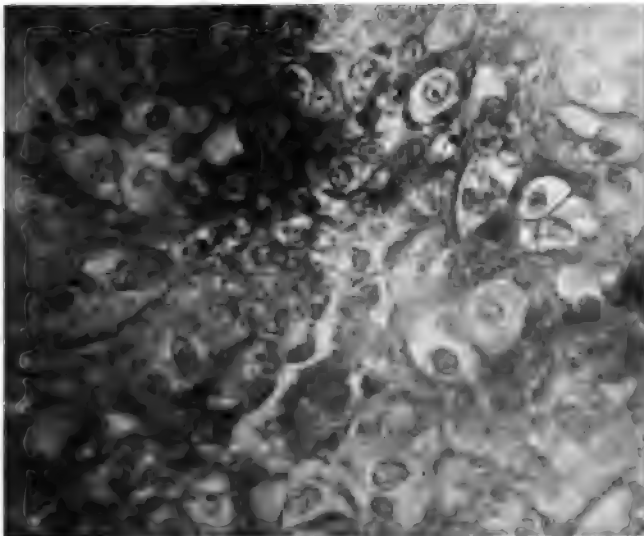
Fig. 127.—(A49100.)   250 D. mag. of cancerous area shown in Fig. 126.   Large polyhedral cells,
20 microns in diameter; pale-staining, slightly eccentric nuclei; very little intercellular substance.

vary somewhat but are usually about 15 microns in diameter.   In
other words, in the same section one may see cells which are normal,
others which are inflammatory, and still others which, apparently
as a result of prolonged irritation, are distinctly neoplastic in char-
acter.   If there is a line of demarcation between certain stages, or
phases, of a chronic inflammatory process and neoplastic forma-
tion, it is, at times, very indistinct and it is difficult, if not impos-
sible, to say where normal evolution stops and neoplasm begins
(Fig. 128).   Or, in other words, the stages of a cell under the

influence, or as a result, of irritation which is constant and pro-
longed seem to be—(1) Normal; (2) inflammatory; (3) hyper-
plastic, or (4) neoplastic (either benign or malignant).

In all the cases studied one may see destruction of the kidney
varying in degree from an involvement of a small portion in some,
to that of the entire organ in others.   In those in which some of the
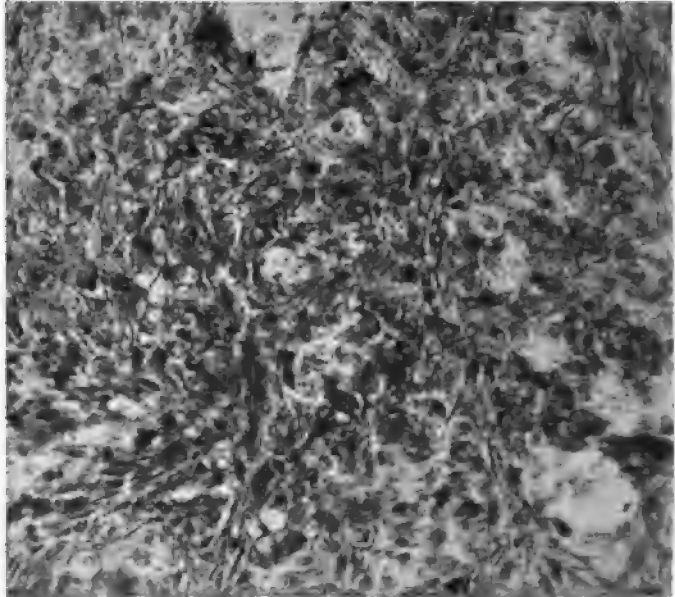
Fig. 128.—(A7569.)   250 D. mag. through area of inflammatory and neoplastic cells.   Tubules
are very small and greatly diminished in number.   The lining cells are spheric, with large, deeply
stained nuclei, scanty protoplasm; surrounded by well-defined strands of connective tissue with oval
nuclei.   At other times they are disposed irregularly.   Cancer-cells at times mimic the renal tubules
in their arrangement of cells supported by delicate threads of connective tissue.   The cells are poly-
gonal, protoplasm very finely granular, limiting membrane distinct.

parenchyma is left there may be seen an interstitial and a paren-
chymatous nephritis; and in some of the specimens are seen areas
of lymphoid infiltration the central parts of which have undergone
necrosis.   In other areas are polymorphonuclear leukocytes, de-
noting abscess formation.   Interstitial changes vary from 1 to 4
on a scale of 4, parenchymatous from 1 to 3 on a scale of 4 (Fig.
129).   In kidneys the seat of stones in many places the epithelial

cells lining the tubules show different stages of degeneration, having lost their vigor.   There is frequently seen hyperplasia of the connective tissue, and the epithelium may be seen to have undergone— (1) Necrosis; (2) cyst formation, and, in some specimens, (3) malignant metamorphosis.   Notwithstanding the work of Kleinschmidt, who says, "Inflammatory changes of the kidney or pelvis of the kidney are not found in my cases," in every case examined, 140 in all, not only in cases of renal stone associated with cancer,
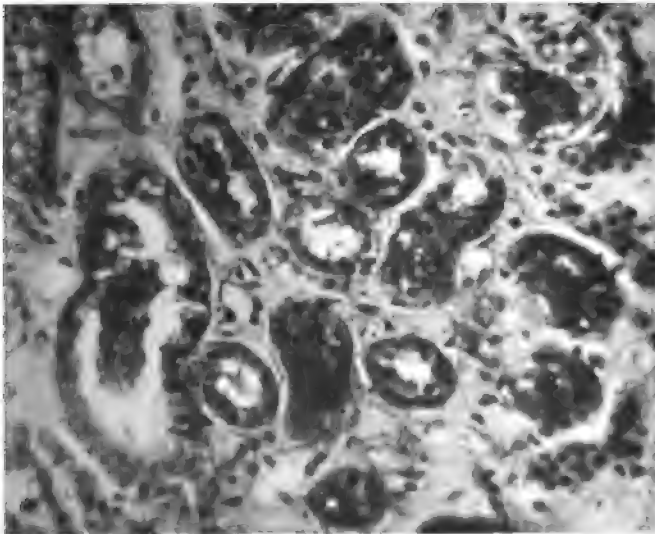
Fig. 129.—(A75806.)   50 D. mag. through area of cut-off degenerating renal tubules.   Shows disintegrating cells lining the tubules, nuclei indistinct.   Protoplasm granular, marked increase in connective tissue.

but also in kidneys containing only stones, inflammatory changes were seen.   They were found in the parenchyma in some cases; in others the process was limited to the pelvis, and in still others, both were involved.   The type of inflammatory reaction varied from that of an acute process in some to a well-marked chronic type in others (Fig. 130).

In several specimens the tubules are dilated in varying degrees, some being four or five times their normal size, and cysts are seen, but not frequently.

'14—18

Stone-pockets are very commonly observed.   Some are microscopic in size.   Other kidneys consist entirely of connective-tissue stone-pockets (Fig. 131).   The walls of the stone-pockets are made up of connective-tissue stroma with lymphoid infiltration lined with two or three layers of cuboid or, in some places, flat cells.

Varying amounts of fat are not infrequently found in the pelvis of kidneys containing stones.   Braasch has called attention to this
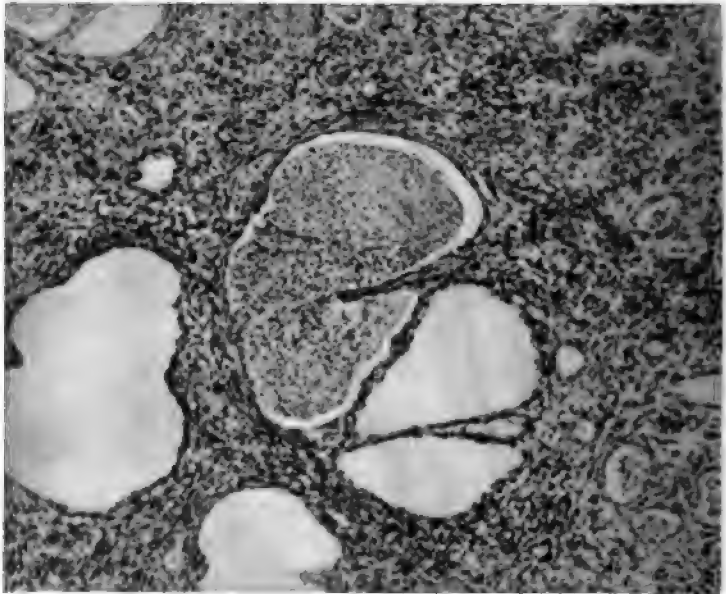
Fig. 130.—(A73915.) 120 D. mag. of section of kidney. Dilated tubules contain pus, polymorphonuclears, and débris.   Walls of connective tissue with one to three layers of cuboid cells whose nuclei are deeply stained; very little protoplasm.

fact.   Smooth muscle-fibers are not infrequently seen in the parenchyma of kidneys containing stone.   In several specimens of this series may be seen spindle-cells with long nuclei, the protoplasm of which is usually granular and stains readily with eosin.   Some of the nuclei are oval;   others are very long and rod-shaped.   These obviously belong to smooth muscle-fiber.   An explanation of the occurrence of the smooth muscle-fibers is found in the fact that in

fetal life the kidney is very rich in smooth muscle, while in adult life it is found only in the capsule and wall of the pelvis. The collecting tubules derived from the Wolffian duct are surrounded by smooth muscle-fibers in early fetal life. These fibers disappear as development advances. At times this disappearance may be in-
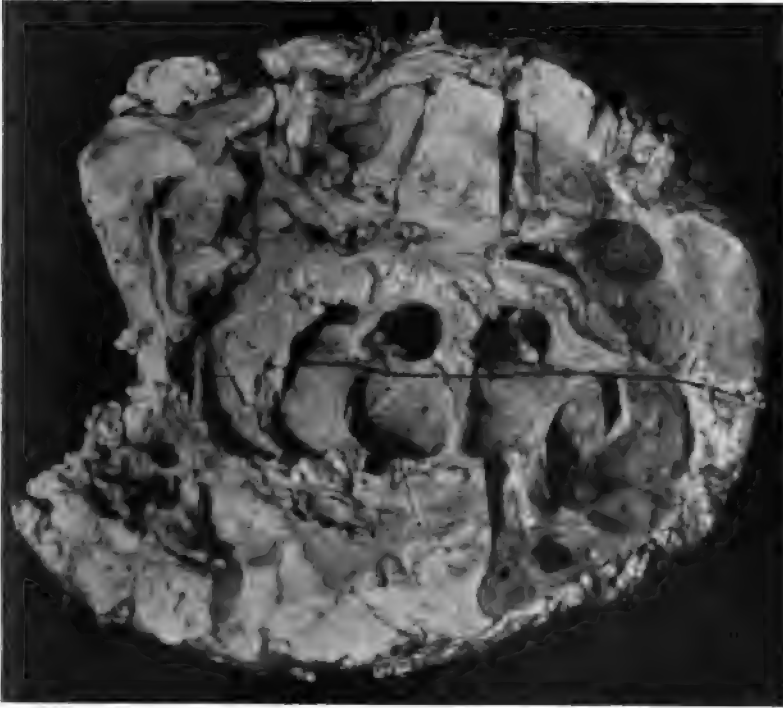
Fig. 131.—(S2907.) Left kidney, one-third normal size. Fat and fibrous tissue throughout. Stones and stone-pockets throughout.

complete and small rudiments of smooth muscle-fiber may occasionally remain in the pyramids (Nicholson). In some of the sections studied these fibers are also seen in the medulla and cortex. Nicholson says that the muscle comes from the same layer of cells which also forms the renal epithelium. This, as shown by Huber, is the mesoblast. Areas in which development has been
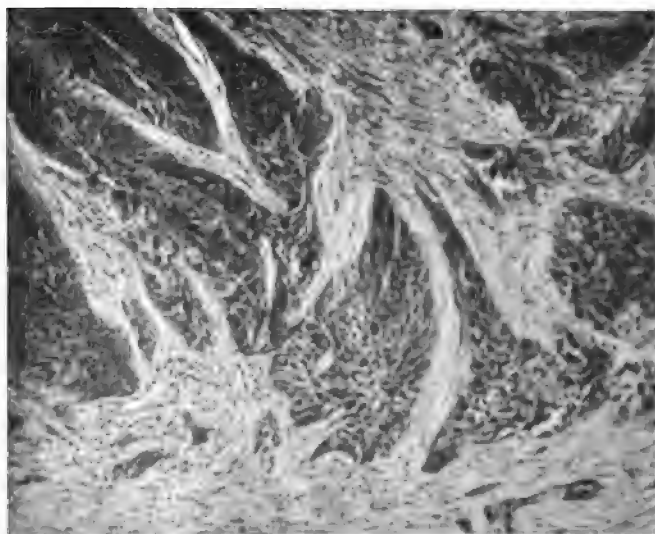
Fig. 132.—(A3809G.) 100 D. mag. of section through squamous-cell carcinoma of renal pelvis. Shows arrangement of cancer-cells and connective tissue.
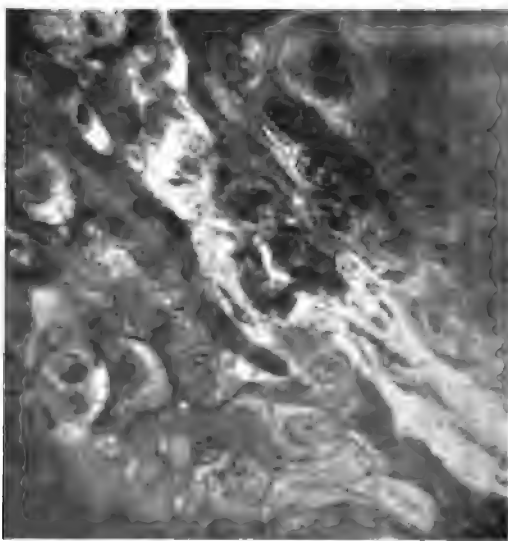
Fig. 133.—(A23253P.) 250 D. mag. of squamous-cell cancer with hyaline degeneration.

arrested at an early period may contain the mother-cell of the epithelium and of the plain muscle.

In squamous epitheliomas arising from the pelvis, of which there are five definite cases in this series, the origin of the neoplasm is probably from the epithelium of the renal pelvis (Figs. 132 and 133). The renal pelvis is derived embryologically from the Wolffian duct, which is derived, in part at least, from the epiblast. Epiblast almost always gives rise to squamous epithelium, there-
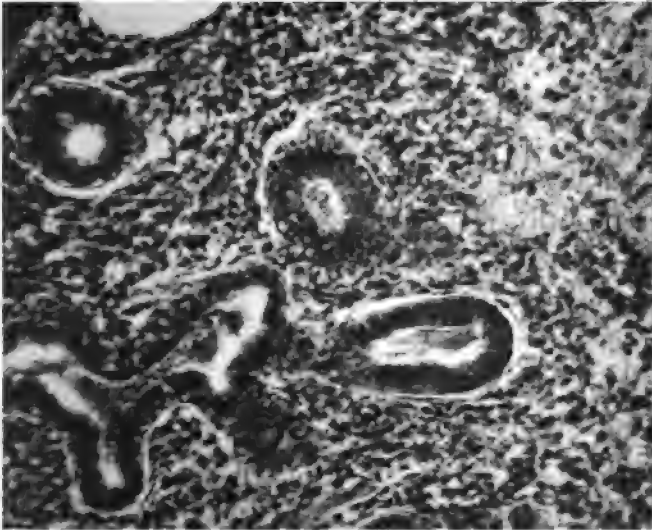
Fig. 134.—(A74679.)   Cancer originating in the tubules, chronic parenchymatous nephritis 2, chronic interstitial nephritis 2, suppurative nephritis, 1.   150 D. mag. of area showing branching cancer tubules, the lining cells which appear to be invading the stroma.   It also shows lymphoid infiltration.

fore it is at least possible that squamous epitheliomas are developed from the epithelium of the renal pelvis. Stoerck says that tumors starting in the renal pelvis are usually associated with conditions of chronic irritation, such as stones.

In one case of cancer associated with stones the neoplasm started in the epithelium lining the tubules. In this particular case it was not ascertained at which part of the tubule the cancer took its origin, but from the glomeruli to the end of the collecting tubules the lining epithelium had undergone various degrees of

degeneration, and in different places along the tubule hyperplasia of the epithelium was seen. In one case (Fig. 134) the tubular "offshoot" was malignant. Thus we see that cancer of the kidney which contains stone may arise from the tubules. In some of these cases colloid degeneration is seen (Fig. 135). At times stones are limited to the parenchyma (Fig. 136). Here the stones are shown in the tubules. There were none in the renal pelvis in this case.
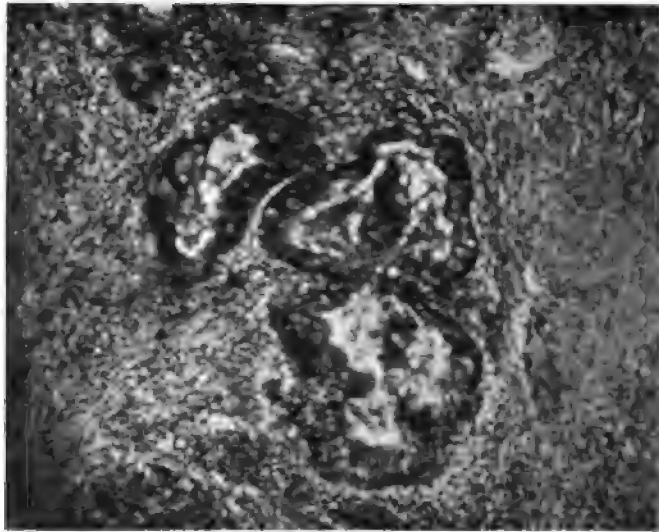
Fig. 135.—(A91370.)   150 D. mag. of section of papillary adenomatous type of cancer, with cells forming acini filled with colloid substance. The cells are supported by delicate strands of connective tissue; the latter sends in strands which, covered with cells, gives a papillary appearance. Lymphoid cells scattered between the acini.

The origin and character of a cell, not infrequently found in kidneys affected with stones, and which occurred in 28 cases in a series of 140, has been somewhat difficult to determine. In some specimens it was not commonly seen, in others it was of very frequent occurrence, and was even found in groups in several specimens. It was a large refractile cell, about 20 to 30 microns in diameter. The cell-membrane was usually distinct, but at times invisible. With hematoxylin and eosin stain the protoplasm was very pale, prac-

tically white, or at most a pale pink, occasionally clear but usually granular, and some of the cells contained vacuoles. The nucleus, not always present and at times fragmented, was about 3 to 4 microns in diameter. It stained with a varying degree of intensity, at times quite deeply. Its border was nearly always well defined. No mitoses were seen in these cells. In general arrangement these
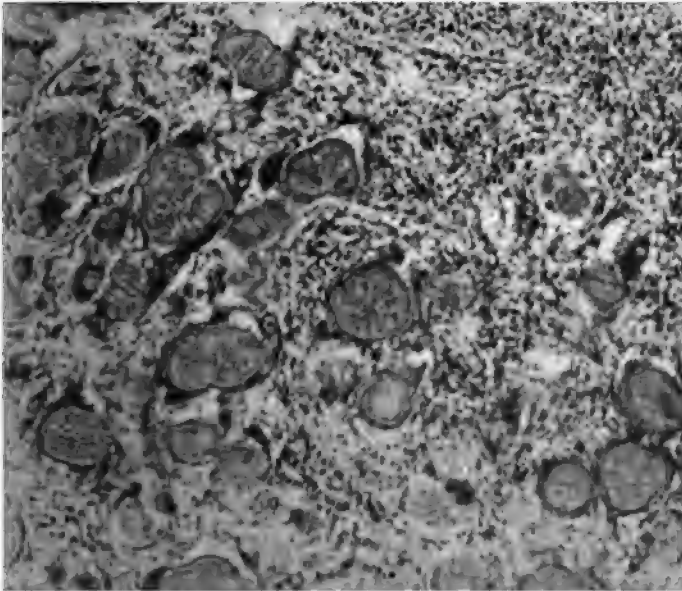
Fig. 136.—(A86712.) 120 D. mag. of section through tubules containing stones. Tubules lined with flattened cells, one to two layers. Stroma increased; lymphoid infiltration. Stones dark-brown color; concentric lamellæ; radial striations.

cells frequently gave an appearance somewhat resembling a meso-thelioma (so-called hypernephroma). They were often arranged in columns along fine strands of connective tissue, which, at times, supported engorged capillaries (Fig. 137). The engorged capil-laries, however, were of infrequent occurrence. In many speci-mens lymphoid cells were seen, varying in number from a few cells to a marked infiltration among the clear cells. Fibroblasts were also seen scattered among the delicate strands of connective

tissue. In some of the sections were red blood-cells interspersed among the clear cells. In some places these groups of cells were surrounded by well-defined bands of connective tissue; in others, a few of the clear cells were found scattered between the renal tubules. Several sections showed cells somewhat similar to these, but they were found in infarcts and were apparently derived from connective-tissue cells and probably largely hydropic in character, since they contained very little fat. From the large, deeply staining nucleus, distinct nuclear and cell membranes, and the fact
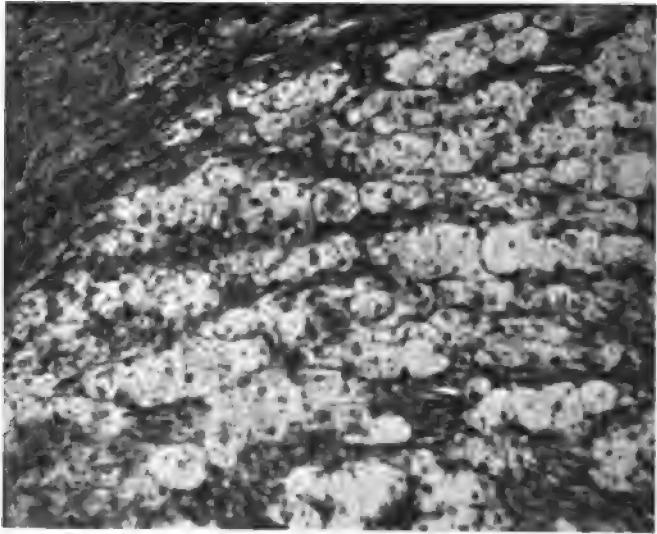
Fig. 137.—(A69689.) 250 D. mag. of section through area of "fat-hydropic" cells arranged in columns, resembling a mesothelioma. Cells supported by strands of connective tissue in which are seen lymphoid cells.

that the protoplasm was light in many cells it was presumed that the cells just described were embryonic in character.

Zebbe describes similar cells and says they may arise from connective tissue, endothelium, or from phagocytes; that they are found in large white and contracted kidneys, but not in acute nephritis nor in diabetics; that they are similar to cells found in the lung and thyroid and Grawitzian tumors (mesotheliomas); and that they are peculiar to the kidney under certain conditions.

Fig. 138 shows this cell in an early stage of development.   Here it seems to be in a renal tubule in which all the cells are of the same type.   They contain granules which stain with fat, as do the cells from other cases which are more advanced (Fig. 137) and are arranged in masses or columns.   They are not found in normal adrenals, but are similar to cells found in mesotheliomas.   They are found in the kidney, are of renal origin, and appear to come from the renal tubules.   They are found in kidneys containing stones, and also in kidneys containing stones and cancer.

TABULATED SUMMARY OF CASES OF RENAL CANCER ASSOCIATED
WITH RENAL STONE REPORTED IN THE LITERATURE

Author	Number of Cases	Cancer	Stone
Ransohoff.............1		Duration twelve months.	Duration much longer.
Noble and Babcock.....1 ? Collected 23		Papillary in pelvis.	....
Albarran and Imbert....3 personal.		All in adults.	....
Nicholich.............1		Papillary in pelvis.	Several.
Minot................3		Papillary in pelvis.	Multiple.
Oraison and Nodal 2		....	
Porter...............1		....	Fifty-three years' history. Weight, 1920 grains.
Deaver...............1		Ureter.	Ureter.
Rafin................3		1. Epithelioma. 2. Mesothelioma. 3. ?	....
Lacassagne...........1		Pelvis.	....

In reporting the foregoing cases the authors dwelt largely on the clinical problems and very little on the pathologic aspects.

It is at once seen that cancer associated with stone in the kidney is not of common occurrence, 3 being the largest number of cases hitherto reported by any author.   Albarran and Imbert collected and reported 26 in two or three hundred renal tumors.

In the Mayo Clinic, since April 5, 1905, that is, in nine years and six months, there have been removed 140 kidneys containing stones, and of these, nine also contained cancer, or about 6.5 per cent.   During the same period six nephrectomies were done for cancer of the kidney, one of which was metastatic.   The proportion, therefore, is 9 cancers of the kidney associated with stones, to 5

cancers without stones, or 64+ per cent. for the former and 35+ per cent. for the latter.   This is about the same as in gastric cancer developing on a gastric ulcer, and of other cancers developing at the site of chronic irritation.

Tuberculosis was found in only 1 of the 140 kidneys containing stones.

Amyloid degeneration was found in 4 cases.

. Polycystic kidney was found in 1 case.
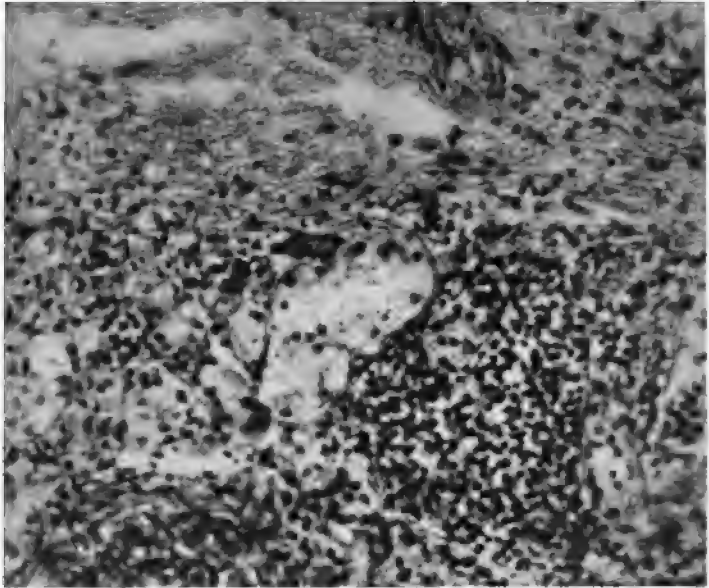
Fig. 138.—(75542.)   250 D. mag. showing early stage of "fat-hydropic" cells seen in the renal tubules (fat stain).

The equilibrium or mutual counteraction between remission of cell multiplication and indefinite reproduction is very sensitive, and until this is better understood, the nature, development, and treatment of cancer will remain an enigma.   Until the origin and development of cancer has been assigned to some definite cause, individuals will continue to accept or to reject theories according to their own ideas.   Certainly some are improbable, while, on the other hand, some have all the appearance of probability and seem almost certain.   From the above study, therefore, it has seemed

useless to even attempt a consideration of the relative merits of the different hypotheses.   However, from clinical and, more particularly, from pathologic study, one must admit that irritation is a strong etiologic factor in the development of renal cancer.

SUMMARY

1.   Renal epithelium (tubular and pelvic) not infrequently regenerates.

2.   Renal tubules regenerate not infrequently as a whole.

3.   The stages of development of renal epithelium under the influence of or as a result of irritation which is constant and prolonged are—(a) Normal; (b) inflammatory; (c) hyperplastic; (4) neoplastic (which may be either benign or malignant).   In the kidney there seems to be no distinct line of demarcation between certain stages or phases of a chronic inflammatory process and neoplastic formation, and it is impossible to say where normal processes cease and neoplastic processes begin.

4.   The preparatory phenomena of renal new-growth seem to take place not in the area actually irritated, i. e., not in the area which shows actual inflammatory reaction, but just beyond the same.

5.   Even if heredity plays the same rôle in human cancer as it seems to play in mouse cancer, chronic irritation in the kidney is still of very great importance in that it determines the location of the neoplasm.

6.   There is, at times, an attempt on the part of the neoplasm to mimic the structure of the kidney by a columnar arrangement of cells and the formation of a lumen.

7.   Renal cancer develops from the epithelium both of the pelvis and of the tubules.

8.   In all specimens studied the kidney in some portion showed an inflammatory reaction.   The destruction of the renal substance varied in degree and was brought about by interstitial or parenchymatous changes or both; and suppuration was of frequent occurrence.

9.   The epithelial lining of renal tubules may, under the influ-

ence of renal stone, (*a*) necrose, (*b*) form cysts, or (*c*) become malignant.

10. After having seen the gradual changes from normal tissue to inflammatory, from inflammatory to hyperplastic, and from hyperplastic to neoplastic, it appears probable that the chronic irritation brought on by the stones was the direct cause of the cancer.

11. In all the cases of renal cancer associated with renal stone a large, light, fat-containing cell is found, sometimes singly, sometimes arranged in groups, and sometimes in definite columns. It has its origin in the tubules of the kidney. Further study will be made of this cell.

12. Of the total number of kidneys with cancer removed, 64+ per cent. were associated with stones and 35+ per cent. were without stones.

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FACTORS WHICH DETERMINE THE ADVISABILITY OF PROSTATECTOMY*

WILLIAM F. BRAASCH

Considerable difference of opinion has existed between European and American surgeons as regards the symptoms which indicate the necessity for prostatectomy. The generally accepted principle abroad was that operation was indicated only when some complication rendered non-surgical treatment difficult or impossible. Consequently, operative relief was not given the patient until long-standing residual urine or infection may have caused degenerative changes in the kidneys and other organs. Recently, however, this attitude has been modified by the more progressive European surgeons. American surgeons, on the other hand, have generally taken the stand that prostatectomy is indicated as soon as there is evidence of persistent residual urine. The following conditions, however, may be present and render the advisability of immediate prostatectomy questionable: namely, renal insufficiency, infection, lithiasis, atony of the bladder, and carcinoma.

Renal Insufficiency.—It is well known that residual urine, even in moderate amount, may cause serious interference with the renal function. However, such renal disturbance, while accompanied by many of the symptoms and clinical indications of true nephritis, is often quite different in that it is dependent on local conditions and may usually be rendered temporary by proper treatment. It is generally accepted that drainage of the bladder is necessary in the presence of residual urine to restore the impaired renal function. However, the degree of residual urine which necessitates drainage

remains a disputed point. It has been our experience that it is best to drain the bladder, even though it contain but two or three ounces of residual urine. The amount of residual urine frequently fluctuates, depending upon the degree of prostatic obstruction. Consequently, although only an ounce or two of residual urine may be present at the time of examination, previously the amount may have been much greater. As a rule, catheter drainage through the urethra is indicated for a small amount of residual urine, while with large amounts, particularly when not infected, suprapubic drainage is preferable when possible. Drainage of the bladder is usually accompanied by the well-known group of symptoms: namely, loss in weight and strength, anorexia, nausea, nervousness, headache, etc., all largely dependent on acute renal insufficiency. After varying lengths of time the renal function improves and the above symptoms disappear. The question then arises: Is operation now advisable?

We have recently been led to believe that the best method of ascertaining the degree of renal function is by means of renal functional tests. It is generally accepted that renal dye elimination and the estimation of urea, both in the blood and in the urine, enable one to determine whether or not the patient is in a suitable condition for prostatectomy. It would seem that the present marked tendency to substitute laboratory data for clinical examination is uncalled for. While functional tests are of clinical interest, and may be of value to a limited degree, they should not diminish the importance of the patient's subjective data and those obtained through physical examination. The improvement of the patient's general condition after he has undergone the reaction consequent to drainage of the bladder has, in our experience, been the best guide in determining the advisability of operation. To be more explicit, if the patient feels well, has regained lost weight and strength, and his appetite is good following drainage, he is ready for operation. With such clinical improvement, even though the specific gravity and functional test were very low, the operation would be safe as far as renal functional capacity is concerned. On the other hand, unless such clinical improvement was manifest,

even in the face of high renal functional estimate, it would be best
to await improvement in the condition before operating.   There
remains, however, a small group of cases in which the patient's
general condition does not improve to any marked degree even
after long drainage, and in which, judging from the results of phys-
ical examination, the advisability of operation may be question-
able.   If in this small group of cases the functional test proved to
be persistently low or high, it might influence the advisability of
operation.

   Infection.—Renal infection is a very important factor in the
prognosis of prostatectomy.   On clinical examination it is often
difficult to estimate the degree of infection and the patient's resist-
ance against it.   Purulent residual urine is usually attended by
pyelonephritis, which often persists in spite of drainage of the
bladder and irrigation.   The severest forms of pyelonephritis fre-
quently follow drainage when large amounts of non-infected resid-
ual urine have been present, and is often the cause of death before
the patient is brought to a condition in which prostatectomy may
safely be performed.   A long period of drainage is advisable in
order that the patient may develop resistance against the infec-
tion.   Even with this precaution, and when the renal function is
evidently normal, as judged by clinical and laboratory evidence,
prostatectomy occasionally lowers the powers of resistance against
infection so that the patient succumbs to it.   Urinary antiseptics
and vaccines have not proved to be of much value in the treatment
of such infection.

   Lithiasis.—Stone in the bladder as a complication of urinary
obstruction occurred in 120 (14 per cent.) of the 872 patients on
whom prostatectomy was performed in the Mayo Clinic up to
October 1, 1914.   Stone was found in the kidney in but three of
these patients.   Eighteen of the patients have returned following
operation for stones in the bladder, of which number 12 had stones
prior to operation.

   It would seem that the etiologic factor which causes stone is
dependent on the altered condition of residual urine.   Neverthe-
less, residual urine could hardly be considered the only cause, since

it was present in practically all the patients in whom prostatectomy was performed. Further, stone is frequently found in the bladder without any residual urine being present. Infection could hardly have been the cause, since infection is so frequently present without stone, and since stone is frequently found with little or no evidence of infection. When bladder stone is present, it is usually advisable to first remove the stone and leave a suprapubic drain before attempting·prostatectomy. This is particularly necessary when there is residual urine or marked infection present. When, however, there is no residual urine nor marked infection and the patient is in good general condition, a well-defined hypertrophied prostate may occasionally be removed at the same time as the stone. The stone itself may be the indirect cause of residual urine as the result of temporary prostatic enlargement. In such cases the intravesical portion of the prostate, particularly the median lobe, may appear enlarged and irritated on urethroscopic or cystoscopic examination. This apparent enlargement is often caused by the stone which irritates the bladder and adjacent prostatic tissue so that they become temporarily congested and produce a moderate degree of urinary obstruction. Little or no vesical trabeculation is then seen on cystoscopic examination. Following the removal of the stone, the temporary congestion subsides and the prostate may become so diminished in size as not to cause urinary obstruction.

Atony of the Bladder.—Atonic conditions causing inability to empty the bladder and consequent residual urine are of common occurrence, and for practical purposes may be divided into three classes: (1) Where other evidence of cord lesion is present, as with tabes; (2) where no evident lesion other than atony of the bladder can be discovered, and (3) where the bladder musculature becomes atonic as the result of long-continued dilatation from urinary obstruction. While, as a rule, the prostatic gland is small and apparently atrophic in the presence of a cord lesion, considerable hypertrophy may occasionally be present. The question may then arise to what extent hypertrophy is the cause of the residual urine. When the patient's general condition is otherwise

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favorable and the cord lesion is not advanced, and when there is no evidence of incontinence, the removal of a large prostatic gland might be advisable.

Not infrequently a so-called atonic bladder is seen where no evidence of a lesion in the nervous system can be discovered and when neither digital nor urethroscopic examination shows evidence of prostatic obstruction. This condition is frequently the result of an evident spastic condition of the internal sphincter which may occasionally be relieved through simple endoscopic incision of the sphincter.

With long-standing prostatic hypertrophy, the bladder may become so markedly dilated as to resemble an atonic condition, and there may be a question as to whether the prostate is the only cause of the urinary obstruction. Following the removal of the prostate, the atonic condition of the wall of the bladder gradually diminishes and the bladder usually empties itself in time. Occasionally a moderate degree of incontinence may occur for a short period following prostatectomy. The control may be hastened and rendered certain by exercising the accessory muscles of urinary control, as suggested by Alexander.[1]

Occasionally there may be a moderate degree of incontinence suggestive of cord lesion resulting from inability of sphincteric closure because of a protruding median lobe. After the removal of the prostatic obstruction the incontinence ceases. Incontinence suggestive of loss of sphincteric control may be present with a markedly distended bladder as the result of overflow. Catheterization demonstrates the presence of control until the bladder is again overdistended.

Prior to the use of the cystoscope and urethroscope many bladders have been considered atonic because of absence of enlargement of the prostate palpable per rectum. Cystoscopic and urethroscopic examination has frequently disclosed residual urine to be the result of definite prostatic obstruction which could not have been ascertained in any other way. Although the cystoscope is frequently an invaluable aid in the diagnosis of prostatic obstruction, it should not be used as a routine procedure. In a large

number of cases with well-defined hypertrophy and an absence of other complications cystoscopy is superfluous. In fact, it is contraindicated in many cases, particularly when the gland is very large and a great amount of residual urine is present. Under such circumstances the trauma caused by the cystoscope, in spite of care, has been known to bring on uremia or even death. With the development of the suprapubic operation and its facility for exposure of the bladder the need for preliminary cystoscopy is now less than formerly. The cystoscope, however, will be of great value and may be the only available means of diagnosis when— (1) Urinary obstruction is evident without any apparent cause on rectal examination; (2) with evidence of possible vesical or renal complication, and (3) when the nature of the prostatic gland is doubtful on digital examination.

It is well known that considerable median lobe enlargement may cause a large amount of residual urine with but little enlargement palpable in the lateral lobes. Evidence concerning the size of intravesical enlargement of the prostate obtained through the cystoscope is of considerable practical value when the rectal examination is doubtful or negative. The data concerning median lobe enlargement gained through the urethroscope are frequently of even greater value. I have also observed three cases in which the rectal and cystoscopic examination gave evidence of but slight hypertrophy, while the urethroscope showed a condition of intra-urethral hypertrophy. The two lateral lobes overlapped so as to leave an S-shaped narrow channel between them. As Young[2] has demonstrated, a moderate median lobe obstruction can frequently be removed through the endoscope. Bugbee[3] has suggested that such median lobe obstructions may be removed by means of the high frequency current. With a predominant median lobe hypertrophy the bilateral enlargement is frequently found at operation advanced to a greater degree than was evident on clinical examination, and endoscopic manipulation would have been insufficient.

Malignancy.—Cases of malignant prostate may be divided into three classes, so far as treatment is concerned: (1) Those which are inoperable; (2) those in which partial prostatectomy is advisable;

and (3) those in which complete enucleation may be attempted. The majority of patients having a malignant prostate come to the surgeon when the condition is too advanced to be operable. Either the gland is involved so that enucleation is impossible, or the patient's general condition is such that operation is contraindicated. A palliative partial prostatectomy may be indicated when there is marked urinary obstruction, when the patient's general condition is good, and the process not too far advanced. Enucleation may be attempted when the gland is circumscribed and the patient's general condition is excellent. The well-known carcinoma and the peculiar position suggestive of posterior lobe involvement usually render the diagnosis certain. Occasionally, however, it is impossible to recognize the malignant nature of the gland on clinical examination. A hard, fibrous adenoma with nodular areas may clinically simulate carcinoma. As Young[4] has demonstrated, cystoscopic evidence may be of value in the recognition of doubtful malignancy. It has been my experience that the data gained by urethroscopic examination are often even more valuable. With benign hypertrophy, a distinct sulcus between the two lateral lobes is visible through the urethroscope; with carcinoma, this depression is absent. In its place may even be seen a median elevation of the floor of the urethra, with considerable longitudinal narrowing of the lumen. The urethra, moreover, will have an eroded appearance and bleed easily on introducing the urethroscope.

Prostatic carcinoma does not frequently cause sufficient hematuria to influence the advisability of operation. Occasionally hemorrhage will complicate the situation to such a degree that immediate palliative operation is necessary. Hemorrhage to such a degree that immediate operation is indicated occurs more frequently with benign hypertrophy, as Kolischer has described.

Cystoscopic examination frequently shows a proliferation of the mucosa of the bladder with chronic cystitis which may be so extensive as to simulate carcinoma. The mucosa may appear to be covered with multiple, low-lying papillomas which frequently bleed easily. The condition is due to inflammatory hypertrophy

of the vesical mucosa as the result of long-standing infection. Usually the condition may be differentiated by overdistending the bladder, which will flatten out the inflammatory hypertrophy so that it no longer resembles papilloma.

In removing carcinoma involving the base of the bladder it may become advisable to remove the prostate together with the portion of the bladder involved. The adjacent prostatic tissue not infrequently becomes enlarged, either because of secondary involvement or inflammatory changes, and unless removed will sooner or later cause urinary obstruction.

A condition which, on digital examination, may closely simulate an inoperable degree of malignancy and still be benign is prostatic abscess. Ordinarily an acute infection of the prostate and periprostatic area would readily be recognized; occasionally, however, chronic prostatic infection may not cause any of the symptoms ordinarily seen with infection. The resulting prostatic enlargement may simulate that of advanced carcinoma, and may be regarded as inoperable. It is only when an acute localization occurs that the real nature of the lesion becomes apparent.

The various observations which I have gathered at random may be summarized as follows:

1. With stone in the bladder it is usually advisable to remove the stone and drain the bladder for a time prior to prostatectomy.

2. Stone in the bladder may cause temporary enlargement of the prostate.

3. Pyelonephritis is a frequent complication of bladder drainage, and a strong resistance should be established before attempting operation.

4. The renal condition prior to operation can be estimated best by clinical evidence.

5. Cystoscopic examination, while valuable in certain conditions, may be the cause of harm if used as a routine procedure.

6. Urethroscopic examination is occasionally of greater value than cystoscopic examination. It is particularly valuable with intra-urethral hypertrophy and with carcinoma.

7. Subacute prostatic infection may simulate carcinoma on clinical examination.

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SURGICAL PATHOLOGY OF THE PROSTATE *

EDWARD STARR JUDD

The prostatic gland originates from five independent groups of tubules which begin to develop about the twelfth week of intra-uterine life. There are from 20 to 70 of these tubules, which are evaginations from the mucous membrane of different areas in the prostatic urethra. In the beginning of their development they are formed into five distinct groups, each comprising a definite lobe of the prostatic gland. The middle lobe lies between the bladder and the ejaculatory ducts, under the floor of the urethra. In rare instances, when this lobe is absent the tubules from the two lateral lobes may be joined in the midline. The median lobe is made up of 9 or 10 large, branching tubules on the floor of the urethra between the bladder and the ejaculatory ducts. In its development the middle lobe is an independent structure, though it is not separated by a capsule from the lateral lobes. There has been much argument on this point. Lowsley,[1] Griffiths,[2] Tandler and Zuckerkandl,[3] and others believe that the middle lobe is independent, while Pallin,[4] Jores,[5] and others believe that the middle lobe is always formed by ingrowths from the lateral lobes. That any one of them may enlarge without involvement of the others there seems to be no question, and many believe that this could not occur in the median lobe if it were a part of the lateral lobes.

The lateral lobes, one on each side, lie at the side and back of the urethra. The tubules of the lateral lobe originate in the prostatic furrows and from the lateral walls of the urethra. There are about 40 tubules in these two lobes, making up the greater part of the

base of the prostate. The lateral lobes are separated from each other by the anterior lobe, the urethra, the middle lobe, and the ejaculatory ducts. They are separated from the posterior lobe by a definite fibrous capsule.
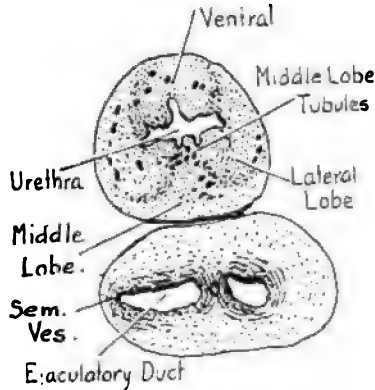
Fig. 139.—Human fetus, 7.5 cm., three months (× 20) (from Lowsley, "The Development of the Human Prostate Gland").
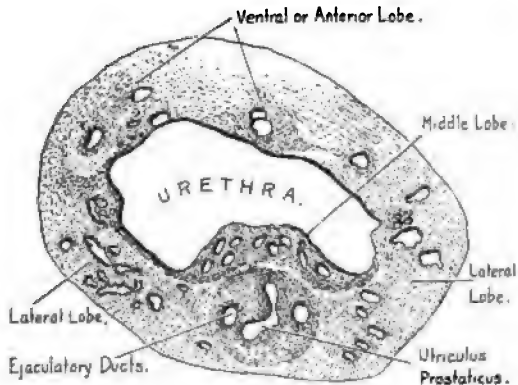
Fig. 140.—Human fetus, 12.5 cm., four months, showing rather definite separation of the middle lobe from the lateral lobes (from Lowsley, "The Development of the Human Prostate Gland").

The posterior lobe lies back of the urethra and the ejaculatory ducts. This lobe is also an independent structure made up of tubules originating in the floor of the urethra below the openings of the ejaculatory ducts. These tubules are definitely separated

from all other parts of the gland and are the part most prominent on rectal palpation.
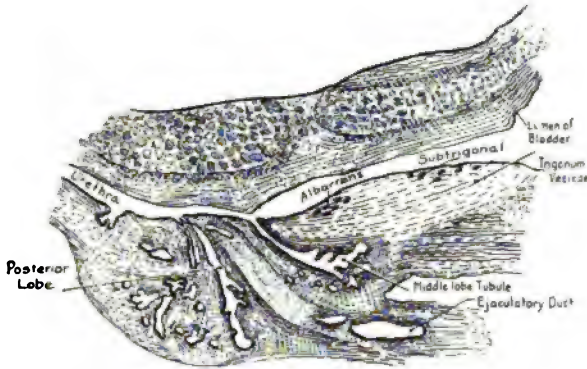
Fig. 141.—Human fetus, 16 cm., prostate (× 15) (from Lowsley, "The Development of the Human Prostate Gland").
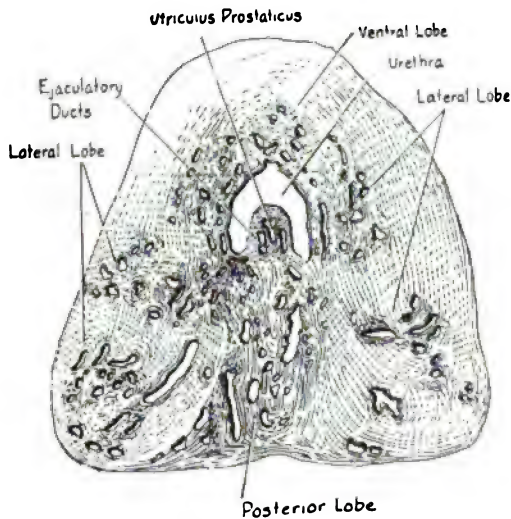
Fig. 142.—Human fetus, 27 cm., seven and one-half months (× 14) (from Lowsley, "The Development of the Human Prostate Gland").

The ventral lobe is formed from the tubules which evaginate from the anterior wall of the prostatic urethra.   It is fairly large in the embryo, though usually decreasing greatly in the early weeks.

The lobe may persist and later become the seat of troublesome adenomas. This, however, is very unusual.

The subtrigonal glands and the subcervical glands of Albarran, which are rarely seen, have not been of great clinical importance in our experience (Figs. 139–142).

ADENOMATOUS HYPERTROPHY

Eliminating inflammations, the most common lesion occurring in the prostate is adenomatous hypertrophy, which is reported to occur in over 34 per cent. of men who reach sixty years of age, though it is symptomless in 15 per cent.

Wilson and McGrath,[6] from a study of 387 specimens of prostatic hypertrophy, concluded that the condition is not a true adenoma formation. They found that fibromuscular stroma is almost always increased in volume. If it is increased in proportion to the parenchyma, the gland is increased in density. This has been sometimes designated scirrhus, but has nothing in common with true scirrhus, since it is not scar tissue. It is not to any great extent muscular, but is most markedly an increase of the fibrous tissue element. When a fresh hypertrophied prostate is sectioned grossly the parenchyma, if increased to any considerable extent, bulges above the cut portions of the stroma, usually presenting a number of prominent whitish nodules. Between these are yellowish or yellowish red, more succulent areas, which on slight pressure exude a cloudy yellowish juice.

The degree of development of the adenomas varies markedly. There may be a single adenoma and fibrous and muscular tissue, or there may be a great many small adenomas and a very little fibrous tissue. At times the most complete closing of the urethra and the most marked symptoms will be produced by a very slight enlargement, and again a considerable enlargement may not cause symptoms or distortion of the urethra.

In reviewing experiences in our clinic and the material at my disposal, adenomatous hypertrophy would seem actually to occur in the lateral lobes as well as in the median lobe of the gland. One

unquestionable case was observed in which the obstruction was due to a single adenoma in the anterior lobe. In this case there was no change in the median or lateral lobes.

Tandler and Zuckerkandl[3] advanced the theory that the process invariably began in the median lobe, and that the median lobe was the only one involved. They also state that prostatectomy is not a proper term, as the prostate is not removed but simply the tumors from the gland. That the prostate is not en-
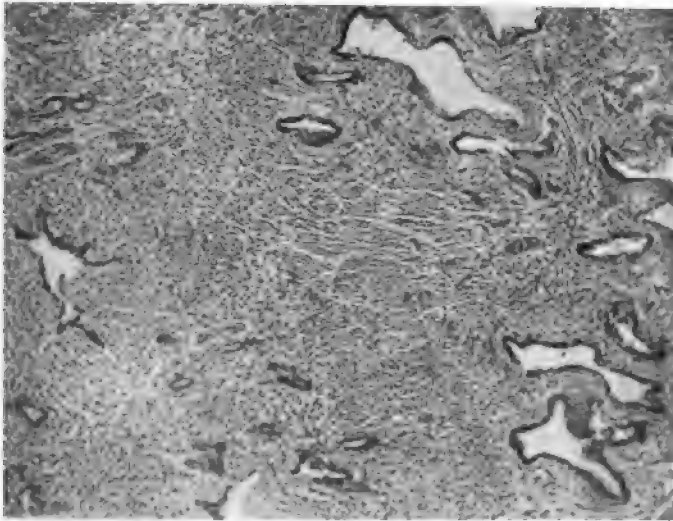
Fig. 143.—Section through the capsule left following removal of adenomas from prostate, showing compressed prostatic tissue.

tirely removed has been proved in several instances by making sections of the remaining capsule. In our experience, this capsule invariably contains prostatic tissue (Fig. 143).

Hypertrophy of the posterior lobe need not be considered, since it is seldom if ever seen. Cancer nearly if not always begins in the posterior lobe. This lobe is absolutely separated from the rest of the gland by a firm fibrous septum. I believe that the adenomas in the prostate bear the same relation to that gland that the adenomas in the thyroid bear to the thyroid. In performing pros-

tatectomy the adenoma is, entirely removed, and with it the part of the prostate on the vesical side of the adenoma. The part of the lateral lobes nearest the posterior lobe is not ordinarily removed in benign cases. By the growth of the adenoma the prostatic tissue is compressed into a firm capsule, sections of which show glandular tissue.

CARCINOMA OF THE PROSTATE

There can be no question that carcinoma of the prostate is usually, if not always, primary in the posterior lobe. If the carcinoma exists alone, there may be few, if any, urinary symptoms until late, because a primary carcinoma is usually small and, extending in the lines of least resistance from the posterior lobe, passes beneath the trigone along the seminal vesicles by a process of infiltration and does not in the early stage project into the urethra or bladder.

In about 50 per cent. of the cases of carcinoma an associated hypertrophy exists, and in the early stages these processes are entirely separate. The obstructive symptoms are caused by the enlargement in the median and lateral lobes. This enlargement, which is composed of adenomatous hypertrophy, may be enucleated from the gland without disturbing the malignant process in the posterior lobe. In certain cases the entire prostate is carcinomatous, and it is impossible to determine positively that portions of it did not represent lobules previously hypertrophied which have become carcinomatous. In these cases the prostate is much larger than when the posterior lobe alone is involved, though the same process of infiltration of the surrounding tissues occurs and there is no definite capsule of demarcation. In these cases the seminal vesicles are always involved.

When benign hypertrophy and cancer exist together, the cancer is usually well confined behind the capsule which separates the lateral and posterior lobes, though, as the malignant process extends, it breaks through this capsule into the benign hypertrophy. In making a suprapubic enucleation in supposedly benign cases,

if the adenomas are unusually attached at any point posteriorly, it is well to have sections made of this attached part as soon as it is removed and, if it shows malignancy, the posterior lobe should also be removed.

MALIGNANT DEGENERATION

In studying 700 specimens of prostates removed in our clinic, Wilson and McGrath[6] found many areas of suspicious change of the hypertrophied process to malignancy, though in no instance was there a positive case showing that benign hypertrophy had become malignant. Young[7] reports that in over 300 specimens removed by prostatectomy he has not found, after careful examination, a single case in which there was an area of cancer in the middle of a hypertrophied lobe, lobule, or spheroid, that is, there was no case in which cancer or cancerous degeneration was present in the interior of a hypertrophied lobe. Whenever a hypertrophied lobe showed cancer within its capsule, it was always found infiltrating the lobe through the capsule from an area of much more extensive and evidently earlier carcinoma. Albarran and Halle[8] mention a condition which they termed "epithelioma adenoid," and thought this due to a malignant degeneration in tissue previously hypertrophied. They found this condition present in 14 per cent. of their clinically and macroscopically benign cases.

Carcinoma of the prostate is probably much more common than is generally believed, because it is infiltrative and not ulcerative in character. Many of these patients die from metastatic carcinoma without the location of the primary focus being discovered. Ulceration into the mucous membrane of the bladder or symptoms of any kind develop late. Often sciatica and pelvic neuralgias caused by infiltration of nerves are the only symptoms. The source of the trouble in these cases is easily overlooked. Because of its infiltrating character the growth is enucleated with great difficulty, and operation gives permanency of relief only in the very early cases.

THE OPERATIVE TREATMENT

The first effect produced by enlargement in the prostatic gland is the deformity of the gland itself. If this deformity is to have a deleterious effect other than its presence, it will soon interfere with the mechanism of emptying the bladder, which in turn will react on the other genito-urinary organs, especially on the bladder and kidneys. The first and most important part of the treatment consists in overcoming as much as possible these secondary changes. If this can be done satisfactorily, the mortality following the operation will be very materially reduced.

The knowledge gained by the more recent investigations regarding the part of the gland most often affected and its relation to the bladder and sphincter muscles has decided most men in favor of the suprapubic or transvesical operation. This operation insures a perfect functional result which is most important in these cases. The serious disadvantage in the suprapubic operation over the perineal is that the opening into the bladder must be made through loose cellular fat tissue in the space of Retzius. This tissue, once becoming infected, is difficult to drain, and, while the infection is not virulent, it may prove very serious in a patient whose kidneys are already badly damaged. The importance of avoiding infection in this space is emphasized by Wade[9] in a recent article. He quotes Page from the records of St. Thomas Hospital, who said that, of 15 fatal cases examined by him, 10 died within a week of operation, the majority from acute local infection or from an acute suppurating nephritis. Wade also states that an analysis of 68 fatal cases occurring in the hospital with which he is associated shows similar results, and strongly indicates that the commonest cause of death after a suprapubic prostatectomy is septic absorption arising out of the wound inflicted.

We have recently endeavored to develop a technic in performing the suprapubic operation which would minimize the possibilities of infection in this space.

TECHNIC

The bladder is cleansed and emptied and the catheter is left in place.   I believe there is less danger of infecting the suprapubic

Fig. 144.—Shows the prostate bulging into bladder and pushing catheter against anterior wall.

space by opening into a dry, clean bladder than into one distended with wash-water (Fig. 144).   The hypertrophied process is enucleated in the usual way and the capsule immediately packed with gauze.   The wound in the bladder is then retracted open by

three Walker retractors.   The catheter is drawn out of the supra-
pubic opening, caught by a clamp, and held to one side (Fig. 145).
The gauze is removed from the prostatic capsule and the bladder
edge of the capsule is sutured with firm plain catgut (Fig. 146).
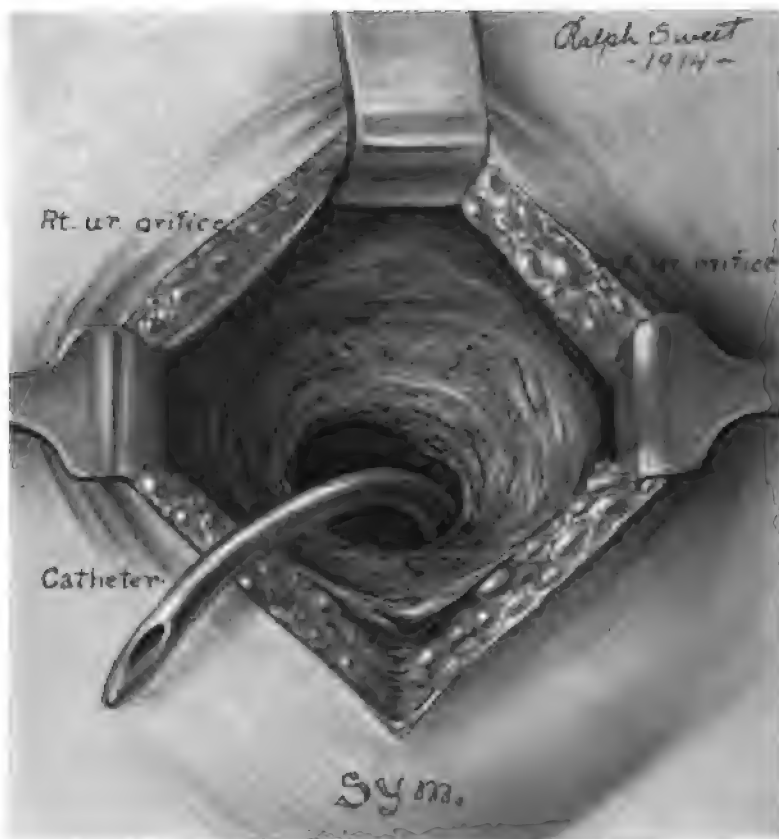
Fig. 145.—Adenomas have been enucleated; catheter pulled out through abdominal incision.

No attempt is made to catch the torn-off end of the urethra, but
the needle is passed as deeply as possible into the prostatic tissue.
By carefully sponging and placing the sutures at the bleeding
points, it is possible in many cases completely to control the oozing.

The clamped end of the catheter is left out of the suprapubic opening in the bladder and the bladder closed tightly around it (Fig. 147). A good-sized hole is cut in the side of the catheter near its entrance into the urethra.
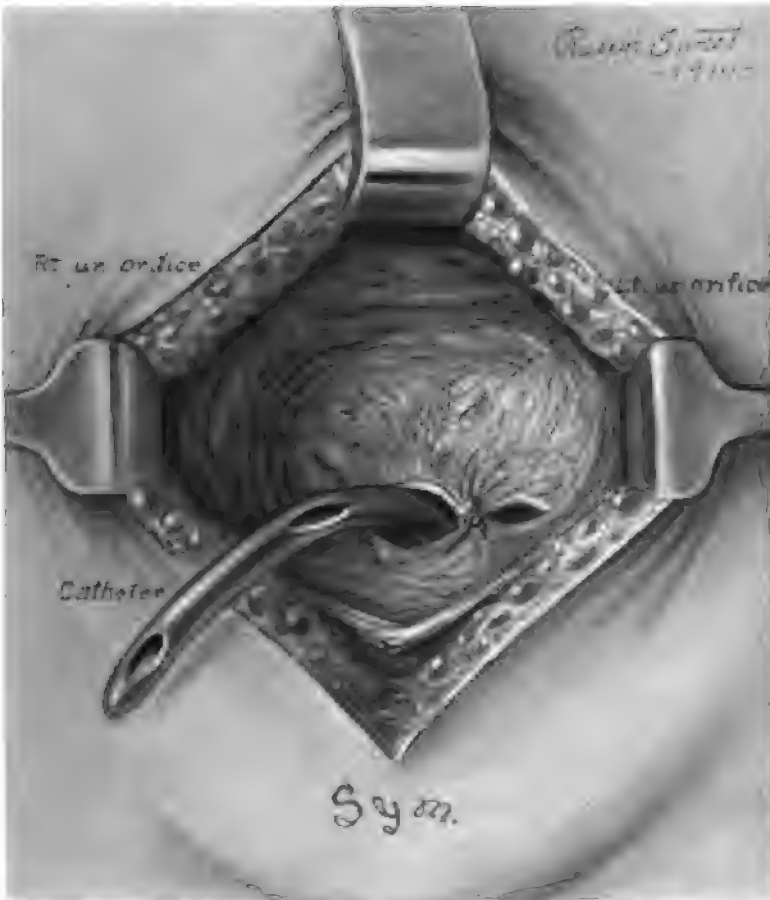
Fig. 146.—Prostatic capsule sutured. Opening inside of catheter just above the urethra.

In a few cases in which the oozing was apparently completely controlled at the time there was some secondary bleeding. This was not serious from a standpoint of loss of blood, but the expel-

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ling of clots was very painful, and in a few cases necessitated intro-
ducing a suprapubic tube into the bladder.   This method of
leaving the catheter projecting through the suprapubic wound in
the bladder is a safeguard against clotting and serious spasm.   As
soon as the urine is free from blood the catheter is drawn into

Fig. 147.—Catheter left outside of wound, which has been closed except where catheter comes
through.

the bladder, where it is left for a number of days.   In many cases
there is no urinary leakage at any time.   In the few instances in
which leakage occurs the urine runs over a surface already granu-
lated, and these granulations prevent infection in this space.

Radical operations for carcinoma of the prostate have not been
entirely satisfactory, principally because it has been impossible

thoroughly to eradicate the trouble without destroying the neck of the bladder, and possibly injuring the anterior wall of the rectum. Palliative operations for cancer of this region are sometimes very satisfactory. I believe, however, that they should be done only when the tumor interferes with emptying the bladder.

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CANCER OF THE PROSTATE *

EDWARD STARR JUDD

It is difficult to estimate the frequency of the occurrence of cancer in the prostate from operative records, since the cancerous tumor in this gland is often very small and may not produce local symptoms. Moreover, in many instances the metastatic lesion is discovered before the primary focus. It is generally reported, however, that one case in five (20 per cent.) of prostatic enlargement causing obstruction in old men is due to cancer. The records from our clinic will bear out this percentage.

There have been 878 prostatectomies performed in the Mayo Clinic up to the present time, December 1, 1914. In 93 of these cancer was found. In addition to these (from January, 1910, to December 1, 1914) 84 cases were diagnosed cancer, but were not operated on because they were too advanced for any operative procedure or because the chances for cure were not good enough to warrant interference in individuals who were fairly comfortable.

A similar ratio of occurrence is found in the autopsy records. Kümmell[1] reports that in 38,472 autopsies there were 204 diseased prostates, 43, or 21 per cent., of which were carcinomatous, while Gebele,[2] in a report on the material at the Pathologic Institute of Munich, says that 38 per cent., or more than 1 in 3 cases of prostatic lesions, were carcinomatous.

Age of the Patient.—In our series of 93 cases operated on the youngest patient was fifty-one years of age and the oldest eighty-two.

Number between 50 and 60 years			....	21
"	"	60 " 70 "	....	34
"	"	70 " 80 "	....	36
"	"	80 " 90 "	....	2

* Read before the Southern Surg. and Gyn. Assoc., Asheville, N. C., December 15–17, 1914. Reprinted from Surg., Gyn. and Obst., 1915, xx, 274–277.

In our series of non-operated cases there were a few patients just under fifty years of age, but the cancer was too far advanced for operation. The age incidence gives no suggestion as to the nature of the trouble, since it corresponds very closely to that of benign hypertrophy.

Symptoms.—In many cases the symptoms do not differentiate early carcinoma from adenomatous hypertrophy. The pain associated with cancer is usually much more marked in the region of the prostate. It is more constant and is not necessarily associated with micturition. This localized pain is supposed to be due to tension within the capsule. It becomes more marked locally, and also radiates into the extremities and to the back as the disease progresses. Pain of this character does not occur in other lesions of the prostate and is somewhat characteristic of cancer.

There is a marked variation in the *duration* of symptoms. A gradual onset, growing steadily and rapidly worse without attacks of acute retention, would seem to favor malignancy. The onset and length of time of symptoms may be identical with the ordinary case of benign hypertrophy. Nine of our patients had had symptoms only six months, while eight had been troubled more than ten years, and two of these more than fourteen years. More than half of the patients had had trouble between one and four years. In all probability in patients having symptoms for a number of years the early symptoms are due to hypertrophy, which often occurs at the same time.

DURATION OF SYMPTOMS

CASES

6 months or under			9
6 " to 1 year			2
1 year " 2 years			20
2 years " 3 "			14
3 " " 4 "			10
4 " " 5 "			7
5 " " 6 "			9
6 " " 7 "			5
7 " " 8 "			3
8 " " 9 "			4
10 "			5
12 "			1
14 "			2

Frequency of urination was one of the most prominent symptoms and usually the first to appear. In many cases frequency and difficulty were noted at about the same time. The frequency was usually first noticed at night. I believe this symptom becomes most marked in cancer involving the entire prostate. A number of our patients voided every few minutes. Difficulty in urination in cases of cancer is not as prominent a symptom as in the cases of benign hypertrophy. It was present, however, in all but 14 of the 93 cases. In three there had been complete retention, and a suprapubic stab drain had been made previous to their coming to our clinic for examination. One patient had suprapubic drainage made two years before coming for operation, and had passed no urine through the urethra during that time. Only two of our patients complained of dribbling. Dribbling was more common in the cases of benign hypertrophy.

Blood in the Urine.—Hematuria was present in 21.9 per cent. of the cases. One patient had noted blood in the urine every day since the symptoms began three years previous. In most of the cases the amount of blood was small and noted only occasionally; it was a comparatively late symptom, being noted at most only a few months before the patient came for examination. In none of the malignant cases was there a sharp hemorrhage or the passing of clots which occasionally occurs in benign hypertrophies. Bleeding did not occur in any of our early cases.

Forty-nine of our patients had used a catheter: 19 had used it for one month or less. In several instances it had been used only once or twice. Three patients had been using a catheter for about one year, one for two years, one for four and one-half years, one for seven and one-half years. One had a permanent suprapubic drainage for two months and one for three months.

It has been interesting to note, but difficult to explain, that in our cancer cases as a group the specific gravity of the urine has been unusually low, in many instances ranging from 1002 to 1005 in individuals generally in good health.

Aside from the character of the pain, which in cancer is apt to be constant and independent of micturition, the symptomatology

of cancer in the early stages is almost identical with that of benign hypertrophy, and the physical examination may reveal the first signs of malignancy.

Physical Findings.—A general physical examination usually shows a healthy, robust individual. Rectal examination may reveal a small prostatic gland, or if hypertrophy is associated with the cancer, the enlargement may be quite marked. If on palpation the surface of the prostate is rough, with hard nodules, it is always suspicious, since in the benign cases the prostates are nearly always smooth unless there is associated inflammation or calcareous deposits in the substance of the gland. In benign cases they are often lobulated, though their surfaces are smooth. In cancer, if the surface is smooth, the prostate is very hard.

It is sometimes impossible to discover malignancy when it is associated with hypertrophy, or to distinguish malignancy from chronic inflammatory prostatitis. In six of our cases the gland was soft, due to the fact that adenomatous hypertrophy predominated and the cancer was not felt. In many of our cases a hard nodule could be felt in one lobe while the other showed no changes.

The characteristic cystoscopic picture is a small prostatic bar unless adenomatous hypertrophy exists at the same time. The mucous membrane of the urethra or bladder is not ulcerated, except in the late cases. Cystoscopic examination is of great aid, especially in ruling out those cases too advanced for operation. However, this examination should not be made in evidently hopeless cases, since the reaction following may be quite severe.

The chief factor in the clinical diagnosis of cancer of the prostate, whether or not it be associated with other conditions, is an irregular, hard "feel" to the surface of one or more lobes of the gland. The type of pain may be suggestive, but is not diagnostic.

A study of our specimens removed at operation showed that in about 75 per cent. the cancer was associated with hypertrophy, and in the remaining 25 per cent. the cancer occurred in prostates in which we were not able to find evidence of hypertrophy. In the group of cases associated with hypertrophy the symptoms and findings were often those characteristic of benign hypertrophy, and in

several instances the cancer was not discovered until the specimen had been carefully sectioned. In these cases the malignant process apparently always started in the posterior lobe, and often was distinctly separated from the rest of the gland, which was not involved. The tumor produced by benign hypertrophy in some of these cases is quite as readily enucleated as in the ordinary case, and unless the posterior segment is enlarged, the malignant process may easily be overlooked. This error has occurred once in our experience. A large bilateral and median hypertrophy was removed in the ordinary way. At the time of the patient's death, a few weeks later, the wounds were healed and the functional results were good, considering the short time that had elapsed. At autopsy a small hard cancer entirely capsulated was found in the posterior lobe. I believe that the cancer in this case had nothing to do with the fact that the patient did not live longer, but the experience served as a good lesson, and since that time, in every supposedly benign case, after removing the hypertrophied lobes the remaining posterior lobe and posterior part of the capsule are carefully palpated for any evidence of hard and irregular nodules. If the hypertrophied part is more firmly attached posteriorly, or shells out with difficulty, there is always suspicion of carcinoma. If the cancer alone exists in the prostate, it is usually easier to distinguish. The tumor is small and hard, and seems to involve the entire gland. In such cases the patients have considerable constant pain not associated with urination unless there is tendency to stricture, a condition which is not uncommon. The growth does not often extend into the bladder, so that from a suprapubic exposure the bladder may appear quite normal. If an effort is made to pass a finger down into the prostatic urethra, a firm hard rim is felt, and if we try to remove this rim, it is found to infiltrate into all the surrounding structures and cannot be removed except in small pieces. These cases are the least favorable for operation. Often in the apparently early cases the malignancy extends beneath the trigone into the seminal vesicles and as high as the ureteral orifices.

Treatment.—Radical operations for this condition have gained favor very slowly, not because it is impossible to remove the growth with a reasonable degree of mortality, but largely because it is

impossible to do a thorough radical removal of the cancerous prostate and the adjoining part of the bladder without completely destroying the mechanism of urinary control. We must also consider the fact that the conservative prostatectomy may cure a certain percentage of the early cases and at the same time give satisfactory functional results. Before undertaking the radical operation the patient should understand that he will have no control of his urine. We see very few people who are at all comfortable with a total incontinence of urine.

Patients who are incurable but fairly comfortable, either with or without the catheter, should not be operated on, though certain of these who have not used catheters should be advised to do so, since they may be made more comfortable by its use. When the patient's symptoms are extreme or the use of the catheter causes great pain, even if the prospects for complete cure are not good, they should have a palliative operation. In many of the cases the obstruction to urination is due to a benign hypertrophy. Removing the obstruction and also a part of the cancer will entirely relieve patients for a time, and they will be much more comfortable than with any other procedure.

The mortality under these circumstances is little more than in the benign cases, the functional result is quite as good, usually the wounds heal just as promptly, and the pain is entirely relieved. Many of these patients live several years in comfort. Kümmell states that these patients receive benefit from x-ray and radium.

End Results.—Through correspondence and personal communication we have been able to trace 82 of the 93 patients operated on. In all these an ordinary prostatectomy was done by either the suprapubic or the perineal method. Of these—

```
 8 lived more than 3 years
12   "      "     "   2  "
13   "      "     "   1 year
24 died within the first 6 months
 5   "    time unknown
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Patients still living after 6 months....................... 3
    "       "      "      "    1 year....................... 7
    "       "      "      "    2 years...................... 4
    "       "      "      "    3  "      ..................... 3
    "       "      "      "    4  "      ..................... 2
    "       "      "      "    9  "      ..................... 1
```

The patient who is living and free from symptoms nine years after the operation had a very small cancerous nodule removed. Many of the patients living at the present time are entirely free from symptoms. Three who were operated on within the year, yet more than six months ago, are well. In the cases of recurrence hematuria was one of the first evidences of the recurrence. Difficulty of urination was also an early symptom and became rapidly marked, necessitating suprapubic cystotomy in a number of cases. Several patients lived more than three years without evidence of trouble, when there was a return of all their symptoms.

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THE DIAGNOSIS OF EXTRA-UTERINE PREG-NANCY *

A Study of 168 Cases

ROBERT D. MUSSEY

This paper is based on 168 consecutive cases of extra-uterine pregnancy operated on in the Mayo Clinic within the past ten years (July 1, 1904, to July 1, 1914). The first series of 100 of these cases were reviewed by Graham[1] in 1910. In reviewing the histories of the subsequent 68 cases, an effort has been made systematically to note points of value in the diagnosis of the condition.

Extra-uterine pregnancy is a term which embraces all pregnancies occurring outside the uterine cavity, *i. e.*, tubal, including the interstitial type; tubo-ovarian, tubo-abdominal, ovarian, and abdominal. The large majority of these pregnancies are primarily tubal, and thus it is that under the term "tubal pregnancy" most extra-uterine gestations are considered.

The classification of the cases may be said to be based on the symptoms and on the pathologic findings. Davies-Colley[2] has made a division adequate for purposes of differentiation. His classification is as follows:

1. Diagnosis either before or after primary rupture occurs with the ovum still developing.

2. Diagnosis at the time the rupture occurs, *i. e.*, the so-called acute cases.

3. Diagnosis of tubal mole or tubal abortion, *i. e.*, .the subacute or. chronic cases.

A review of the findings in our last series of 68 cases shows that the greater number come in the third group.

We had 19 unruptured cases, 19 ruptured with free blood in the peritoneal cavity, in many of which the blood was old with clots, and 30 subacute and chronic cases.

Of these, the group of acute cases is the easiest to diagnose. For example, one is called upon to examine a woman of the child-bearing age who has missed one or more periods and who has a sudden, severe, tearing, one-sided, lower abdominal pain accompanied by collapse. She is found pale and weak, with a small pulse, sighing respirations, thirsty, and faint. Frequently the abdomen is tender and rigid. Usually there is no fever. Pelvic examination reveals the signs of pregnancy in the changes in the cervix and the discoloration and softening of the vaginal mucous membrane. There may be a definite mass in one side of the pelvis. Most of such acute cases may be correctly diagnosed.

The unruptured cases in our series are comparatively few and are the most difficult to diagnose. Undoubtedly many such are never diagnosed. DeLee[3] says that the diagnosis of extra-uterine pregnancy is rarely made before there is a rupture of the tube or a hemorrhage into it. Hirst,[4] however, made the diagnoses in a majority of his cases before rupture occurred. In many of these cases absorption of the fetus and death occur before rupture takes place. Undoubtedly many such are mistaken for miscarriages.

Our attention is chiefly directed to the subacute and chronic types, the typical picture of which differs somewhat from the acute. There is a similar history of a missed period. The woman may have had morning nausea and may suspect she is pregnant. She has had discomfort in the lower abdomen, with possibly several attacks of severe, cramping, bearing-down pains, accompanied by prostration. This has probably been followed by a vaginal flow, at first profuse and bright red, but later more scanty and of darker color. There may have been decidual discharge. The flow may have continued rather persistently to the time of examination, and may have increased with each attack

of pain. The woman may have lost in weight, may have fever or a history of chills and fever. She looks worn and somewhat pale. Examination determines the signs of possible pregnancy in the increased fullness of the breasts, from which secretion may be expressed. The usual vaginal signs are found. In one side of the pelvis, and slightly back of the uterus, there is a mass which seems to be independent of the uterus and yet is attached to it. Frequently there is the "collar feel" described by Davies-Colley,[2] of blood which has collected in the culdesac around the rectum. In such a case the diagnosis is simple.

In reviewing the histories of cases in this series the cardinal points in diagnosis may be noted as follows: (1) Pain. (2) Disturbed menstruation, making careful history-taking of great value. (3) Data obtained by a pelvic examination.

The average age of the patients in the 168 cases was thirty-one and a half years. Most writers, however, place the average age between twenty and thirty. Our oldest patient was forty-five years, and the youngest fifteen. Sixty-five had not had children and 31 had only one child. The number of children in all averaged a little less than two to each mother. The largest number was seven. The average age of the last child was a little under six years, the youngest eleven months, the oldest nineteen years. Four patients had previously been operated on for extra-uterine pregnancy.

A history of miscarriage was obtained in 50 of the cases. A definite history of previous pelvic inflammatory conditions was noted in not over a score of cases, and a doubtful history in possibly 30 others.

The average time since the last regular menstrual period was nine weeks. The duration of symptoms of either flow or pain averaged five weeks and one day. In three cases of old extra-uterine pregnancy the complaint had lasted for nine months, eight months, and two years respectively. One woman, age forty-four, came complaining of uterine prolapse, having no symptoms of extra-uterine pregnancy. An early unruptured extra-uterine pregnancy was found.

In many of the cases in which diagnoses were not made the menstrual history was not clearly noted. The previous menstruation had been regular in 54 cases, irregular in 9, and painful in 10. In 127 the flow was disturbed. In most of these the flow was rather continuous from the onset, and in only a comparatively few cases was it excessive. The duration of the flow lasted from three days to two months. Pain and flow came at the onset of symptoms in 47 cases, with onset of pain before the flow in 43 cases, an average of fifteen days before flow. The unusual flow came before the pain in 21 cases. In 10 patients, a little over 5 per cent. of the series, no period had been missed.

The character of the pain is of importance. Sixty-seven of these patients gave histories of having severe pain, in 25 cases coming in distinct attacks, 22 of whom had symptoms of shock. Seventy-four had less severe pain; in 13 it was mild. Sudden onset of the pain was noted 15 times. The pain may be described in a variety of terms: bearing down, severe, colicky, constant dull aching, pressing, grinding, tearing, and "sore" pain.

In 19 cases the pain was located in the lower abdomen; in 17 in the right lower abdomen; in 8 in the right iliac fossa; in 4 working down over the abdomen; 11 cases in the left lower abdomen; 14 cases in the rectum, or associated with painful defecation; in 9 cases, in 1 of which the pain worked upward, described as pelvic; in 6 cases the pain was upper abdominal, in 2 of these distinctly working up to the epigastrium and in 2 working from the epigastrium downward; in 3 the pain was in the right hypochondrium; in 1 distinctly like gall-stone colic. In some cases the pain was felt mostly in the back.

Pain was the most constant feature; in only 3 cases was there no pain or discomfort.

The examination of the pelvis is of great value, but here also we find a great variance in description. In 4 histories of cases the pelvic findings were not mentioned. In 1, no masses were felt, and in 2 the examination was recorded as indefinite. Masses were found back of the uterus, to the right or left or in both sides, sometimes as a bulging, occasionally as a thickening or fullness.

In 5 cases the masses were abdominal, in 2 pelvic and abdominal. The mass may be movable or immovable, fluctuating, firm or hard, soft, doughy, boggy, large or small, globular, pulsating, semifluctuating, separate from uterus, or described as connected with the uterus. The size is definitely described in only 4 cases. In 40 out of thé last 64 cases the findings corresponded exactly with the location and description of the mass.

Other factors to be considered are chills and fever, which occurred in 38 of our cases. Nausea and vomiting occurred in 71. The approximate duration of pregnancy before onset of symptoms was about seven weeks.

From a review of the main descriptive points in the diagnosis of extra-uterine pregnancy one finds a wide variance in symptoms and findings. This variance in itself would seem to indicate the difficulties arising in the diagnosis. Many conditions causing disturbed menstrual flow, e. g., normal pregnancy, pregnancy with retroversion, pelvic tumors coincident with intrauterine pregnancy, abortion, especially when coincident with or in consequence of some growth in or near the uterus, pregnancy in the uterine cornua or in a double uterus, and subacute endometritis associated with salpingitis, must be ruled out. Conditions must also be excluded that are associated with abdominal pain, such as appendicitis or abscess of the appendix, salpingitis, dysmenorrhea, ovarian cyst with twisted pedicle, ureteral stone, gallstone colic, obstruction of the bowel, tumor or diverticulitis of the sigmoid, intestinal or gastric perforation, or any condition giving rise to a pelvic mass, such as fibroids, ovarian cyst, hydrosalpinx or pyosalpinx, abscess of the appendix.

In any of these conditions the atypical cases give rise to difficulty in diagnosis, and especially is this true of any pelvic mass associated with discomfort or pain and any disturbance of the menstrual flow.

Quite frequently the differentiation of pelvic conditions associated with disturbed menstruation is by no means easy. With a missed period of pregnancy coincident with uterine deformity or pelvic masses the history of attacks of pain is usually lacking. In

the absence of pain the element of time is of value in determining the diagnosis. One can wait to see if a normal pregnancy is developing. When the period has been missed and the flow begins again, as in abortion associated with some growth in or near the uterus, the diagnosis is often very difficult. Usually there has been pain, the flow is present, and the mass can be felt. The character of the flow is slight, often dark, and usually constant. In miscarriages the flow is generally more marked, a brighter red, and is over in from seven to ten days. The diagnosis may be decided by careful pelvic examination.

A condition which is most often wrongly diagnosed is extra-uterine pregnancy simulating a salpingitis, with an attendant endometritis. There may be disturbed flow, pain, and tumor-mass; there may also be fever. The diagnosis may be decided by the kind of flow with the demonstration of decidua in the discharge. Careful observation over a period of seven to ten days may be necessary to determine this. Signs of pregnancy and the patient's sensation of pregnancy are of value, but may be misleading. The Abderhalden test may prove to be of great value in these cases. Conditions giving rise to severe pain may have to be differentiated. Extra-uterine pain may simulate a gall-bladder colic with an associated irregularity of menstrual flow. The pelvic examination may be difficult and correspondingly unsatisfactory. The mass may be so small as to be overlooked. A careful history may be the only means of differentiation. The condition may be an ovarian cyst with twisted pedicle which defies differentiation. Pain in the rectum or painful defecation, which was noted in 14 of our series of 68 cases, is a valuable point. When present, it seems pathognomonic.

Of the 168 cases in this study, 106 were diagnosed as extra-uterine, though some as doubtful. Twenty-one were diagnosed as pelvic tumor; 4 as appendicitis; 12 as pelvic inflammation. In 10 an exploration was advised of the pelvis, of the ovary and tube, or of the appendix, with no suggestion of ectopic pregnancy. The diagnosis of gall-stones or perforation was made in several cases, sometimes without the suggestion of pelvic examination.

To summarize briefly: First, pain is the chief feature. An attack, and more especially interval attacks, of the peculiar colicky, sickening, low abdominal pain, occurring in a woman who has had a missed or delayed menstruation, should always put one on the alert. The description of the pain should be carefully worked out as to manner of onset, location, degree, and character, and whether it be in attacks or continuous.

Second, flow in its relation to the pain, its amount, consistence, color, odor, and continuance. The missed period, followed by a bright flow which becomes dark and tends to be a small, steady flow, the finding of decidua, the increase with each attack of pain, and the character of flow at the time of examination, are all to be noted. In attacks of abdominal pain simulating colic of the gastro-intestinal tract the careful menstrual history should not be neglected.

Third, the routine pelvic as well as physical examination, noting any signs of pregnancy, as well as any abnormal findings.

Fourth, one should not be misled by the association of chills and fever, with symptoms of pelvic disorder. Careful history taking and careful physical examination cannot be too greatly emphasized.

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UTERINE PROLAPSE, WITH ASSOCIATED PELVIC RELAXATION *

CHARLES H. MAYO

Uterine prolapse, as it is usually termed, is in reality a form of hernia. The great majority of uteri take the retroverted position with the onset of prolapse. The retroverted position seems to be the common one of the uterus in over one-fourth of women, apparently in the majority of them without symptoms due to the position. It is possible for the uterus to undergo some degree of prolapse when it is in the vertical position—in such a case it moves forward nearer to the pubes and encroaches on the bladder space. It is evident that a slight degree of descent of the uterus may occur without necessarily being considered pathologic.

While there are many varieties of operations for the relief of the various types of uterine prolapse, there are only a few principles involved, although various surgeons have made many modifications in technic.

In the majority of cases of retroversion in patients between the ages of twenty and forty in whom the symptoms are serious and growing worse some form of external or intra-abdominal operation on the ligaments to restore the uterus to position is indicated.

For the cases of mild prolapse with retroversion or flexion without other intra-abdominal complications for which an exploration would be advisable a simple Alexander operation on the round ligaments, or some modification of the original technic, has proved very efficacious.

With retroversion and descent difficult to replace because of

probable associated pelvic lesions or other abdominal complaint the true condition of which had best be known, an intra-abdominal operation should be made on the round ligaments. If, as occasionally occurs, the cervix remains too far forward, the uterosacral ligaments or lateral folds of peritoneum should also be shortened effectively to bring the uterus to anteversion.

The interposition type of operation is very effective in the relief of partial uterine prolapse associated with extensive cystocele. We have secured the best results from this method in cases in which there is a firm uterus which does not come out of the vagina in the anteverted position at operation. This usually means an age limit within the forties. This operation relieves cystocele and descent or the first and second degree of prolapse. In the third or fourth degrees of prolapse it should not be chosen. When made before the climacteric, it is advisable to divide and invaginate the tubes at the uterine horns to prevent any possibility of pregnancy occurring with such a misplacement of the uterus. The uterus, being rotated from the extreme retroverted position to an anteversion,—a rotation of 165 degrees,—and the bladder separated from the anterior vaginal wall, the fundus of the uterus takes its place, the bladder resting on the fundus and posterior part of the anteverted uterus. Patients with relaxed vaginal outlet and soft uterus may continue to feel some protrusion and often think the cystocele is still present. If this operation is applied to women in the fifties, with a soft, degenerating uterus undergoing rapid atrophy, and in whom the torsion of the ligaments in anteversion still permits the uterus to be brought out of the body at the operation, it will undoubtedly fail of relief and another method should be substituted. With the interposition operation in such cases we have seen within a few months the whole uterus come out of the · vagina, broadside, followed by the bladder, the condition of the patient then being worse than before operation.

In another class of patients, usually from fifty to sixty-five years of age, where hysterectomy has been made without successfully supporting the cervical stumps or vaginal terminus, prolapse of the vagina with cystocele and rectocele may develop six months to

ten years following the operation. Some of these patients of advanced years are best relieved by total extirpation of the vaginal mucosa, with a complete closure of the vaginal outlet by an extensive restoration of the perineum, leaving exposed only a small area of mucosa around the urethra. Occasionally a suprapubic operation is effective in reattaching the stump of the cervix or upper vagina to the abdominal wall, accompanied by an extensive perineal closure.

The Kocher operation, or some modification of it, is occasionally made upon women in the forties,—in which case the tubes are divided,—but the method is usually reserved for women past the change of life, with atrophied uteri. The operation by this method will probably be successful in those cases in which, when the cervix is grasped and pushed well up, thus restoring the vaginal position, the cystocele is greatly reduced. If, however, the bladder has been torn loose from its uterine attachment and the restoration of the uterus to high position does not elevate it, the Kocher principles of operation alone will not relieve the trouble. As a matter of fact, it may be difficult to perform an operation which will securely fix the fundus of the uterus to and through the abdominal wall. The constant traction tends to cut out the sutures, and while there is a string of adhesions, the full support and elevation which apparently is satisfactory at the time of operation may not be permanent. As in the Murphy modification, the uterus is drawn through the abdominal incision and bisected anteriorly and posteriorly, down to the internal os. Each half is turned outward, and all the mucosa dissected out above the internal os, leaving about a half thickness of the uterine wall. The peritoneum of the abdominal incision and the recti muscles are sutured all around the uterus at the level of the internal os. The aponeurosis is separated from the recti muscles opposite the projecting uterus. Each half of the fundus is turned outward over the recti muscle and beneath the aponeurosis, to which they are secured by three mattress sutures on either side (Fig. 148). The aponeurosis itself and the recti muscles are now closed, and the aponeurosis over the cervical uterine tissue is again caught by two

deep sutures to it. The abdominal wall is closed without drain-
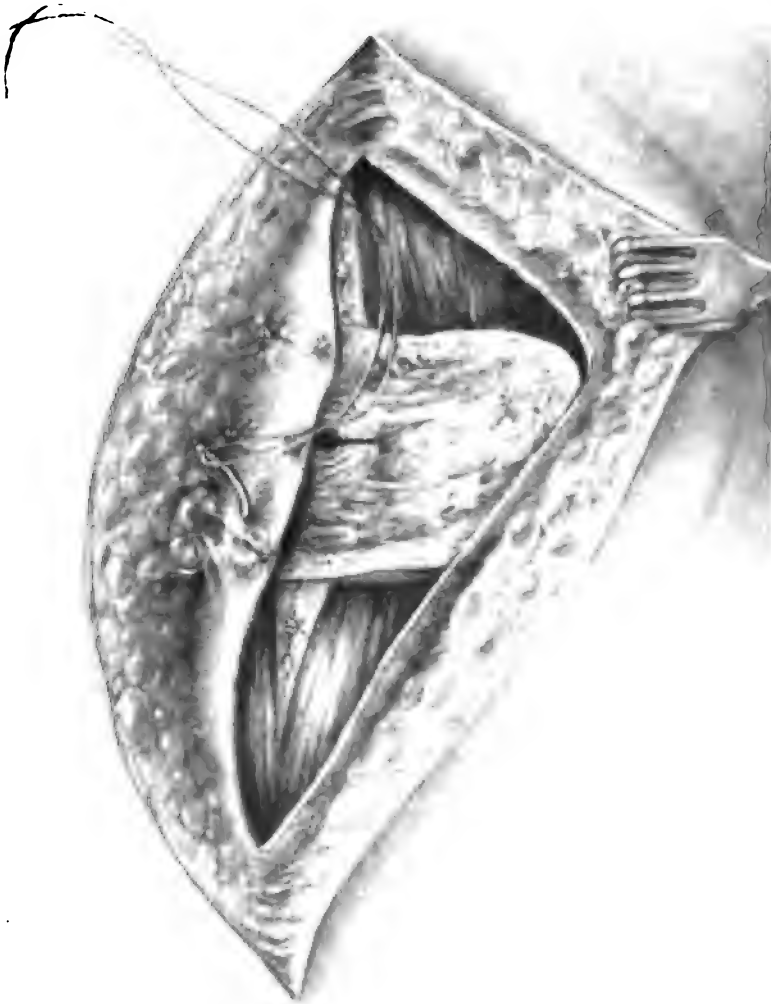
Fig. 148.—Suture of aponeurosis to uterine muscle.

age. The sutures, which include the uterine muscle tissue, should
not be drawn tight, since the tissue easily cuts through. We have

used silk and chromic catgut for sutures. It differs from **J. B.** Murphy's method only in placing the uterine tissue over the recti muscles and under the aponeurosis, leaving thereby a smoother

Fig. 149.—Cross-section of suspension operation.

abdominal wall, and I believe makes a stronger support. After all, it is not the prolapse of the uterus or the varicose ulcers and erosions upon its exposed surface, but the cystocele and the malposition of the bladder, which are the cause of the patient's discomfort.

Such ulcers and erosions as may be found are seldom painful, and the exposed and vaginal mucosa becomes so near like skin that it is probably less irritable than it frequently is when undergoing the senile atrophy of the mucosa of the vagina at the menopause without exposure to the air (Fig. 149).
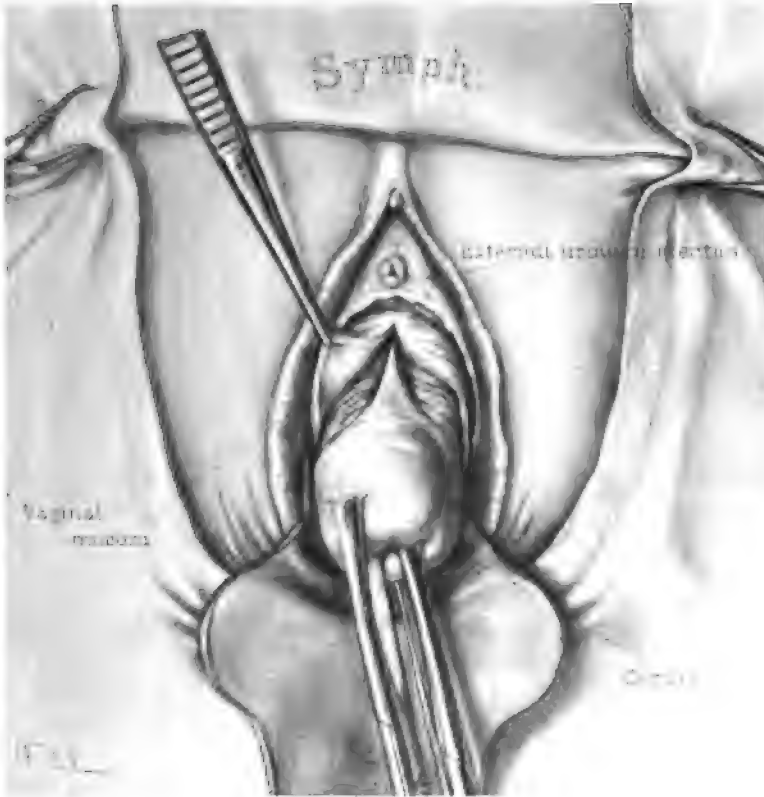
Fig. 150.—Primary pear-shaped incision for vaginal hysterectomy.

For a large group of cases of the third and fourth degrees of prolapse in patients between forty-five and sixty-five years of age, often with atrophy of the uterus and distention of the vaginal outlet, the interposition type of operation is not indicated. For such cases, with separation of the bladder from the uterus and a large

cystocele, in which the Kocher operation is also not indicated, and the atrophy of uterus and ligaments too extensive for any intra-abdominal support to be secured, we have long practised the following very effectual method of securing relief:

The cervix is grasped with two pairs of vulsellum forceps and drawn well out of the vagina. A pear-shaped incision is now made, with its apex one and one-half inches below the external urinary meatus. It passes down each side of the cystocele and around the cervix (Fig. 150). The sides of the incision are grasped, and the vaginal wall readily separated from the bladder by blunt gauze dissection. The apex of the vaginal flap attached to the anterior lip of the cervix is turned down, and the bladder rapidly separated by gauze dissection from the front of the uterus. As soon as the peritoneal fold is reached it is incised and divided laterally. The blunt gauze dissection now separates the posterior vaginal wall from the uterus at the side and on to the broad ligaments. The sharp fork retractors are now used to draw the fundus of the uterus out of the incision, as in an ordinary hysterectomy, and the cervix is restored within the vagina. The broad ligaments are fully spread out on each side. Unless the ovaries are diseased, they are not removed. A heavy hysterectomy forceps with long blades now grasps each broad ligament. The uterus is divided a half-inch from the forceps and two more pairs are applied, one on each side, with their tip catching the culdesac behind the cervix. The uterus is then cut entirely away (Fig. 151). When the tissues are not sufficiently relaxed for easy approximation, a little of the lateral wall of uterine tissue may be left attached to the broad ligament.

If there is any tendency of the sigmoid or omentum to prolapse, it is held back by a long pad of gauze inserted into the peritoneal opening. The pairs of forceps, two on each side, are now approximated laterally, and a running mattress suture of chromic catgut is applied, which passes back and forth behind the forceps completely through both ligaments at such a distance as to tighten the broad ligaments (Fig. 152). An approximation of from $1\frac{1}{4}$ inches to $1\frac{1}{2}$ inches of these ligaments is secured. The method of suture is applied so as to interlock and prevent the inward slipping

of any vessels. When the suturing reaches the round ligament, it
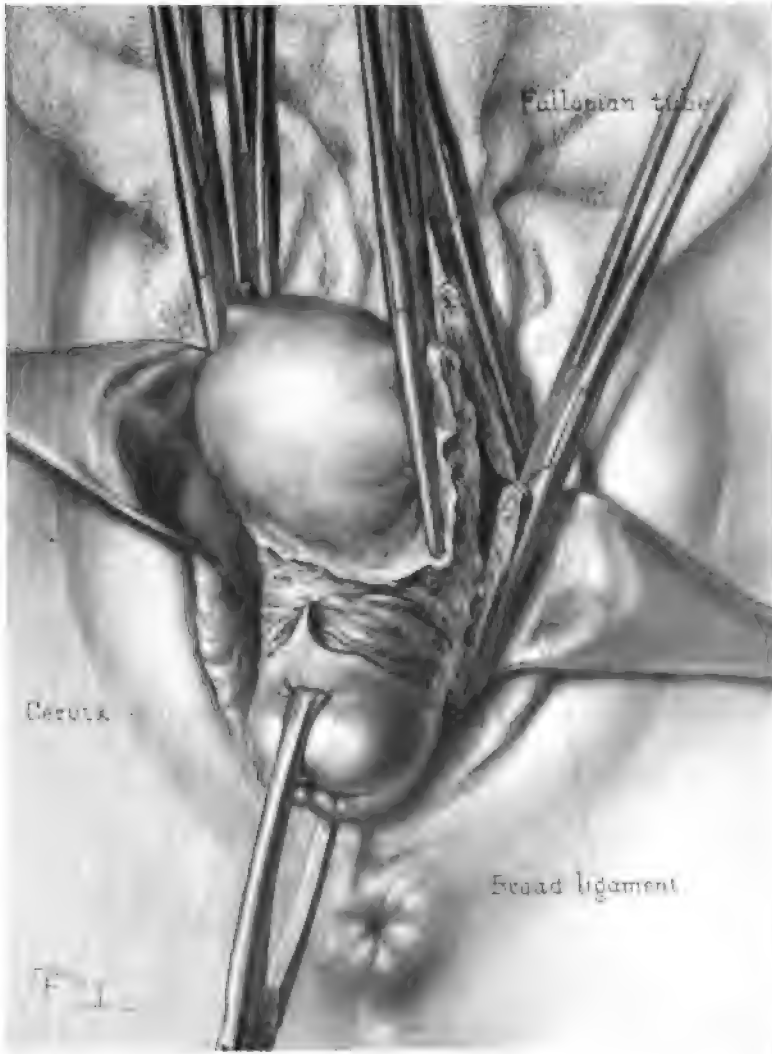
Fig. 151.—Excision of uterus and clamping of broad ligament.

is caught into the angle of dissection where the bladder has been
separated from the anterior vaginal wall. This suturing extends

backward on each side from this point, catching into the broad
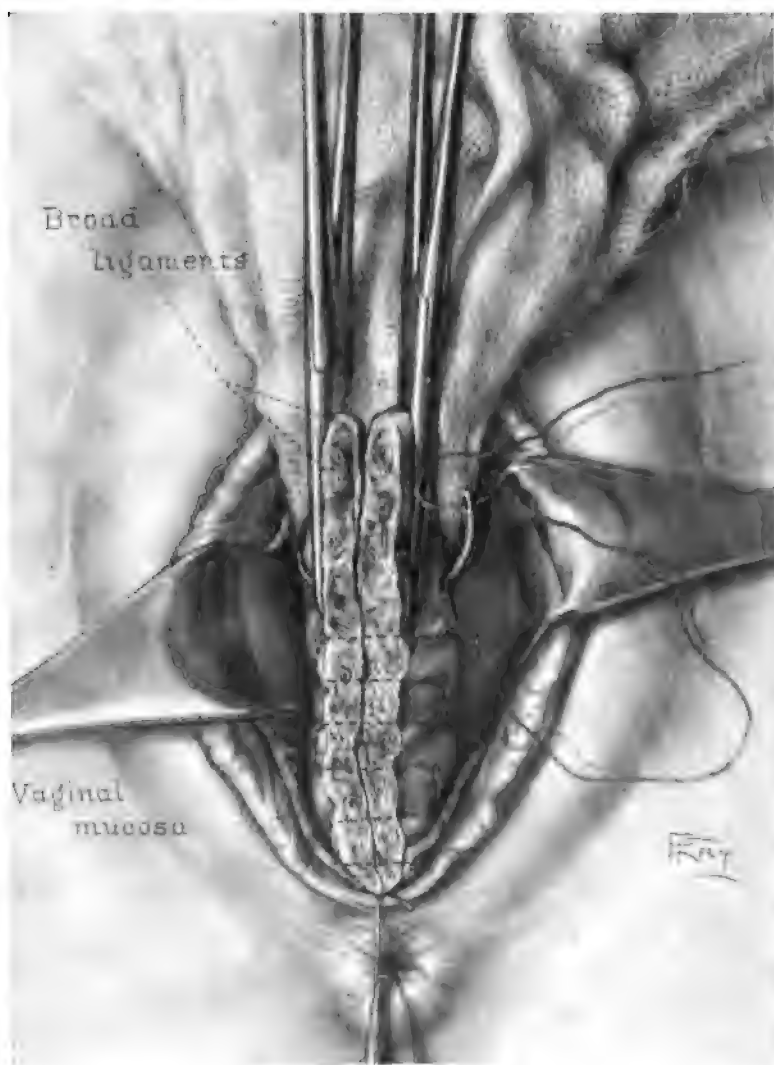
Fig. 152.—Broad ligaments approximated by running mattress suture.

ligaments, and then on each side into the angle of the depth of the
dissection, thus compelling the bladder to rest on the broad liga-

Anterior
vaginal
wall
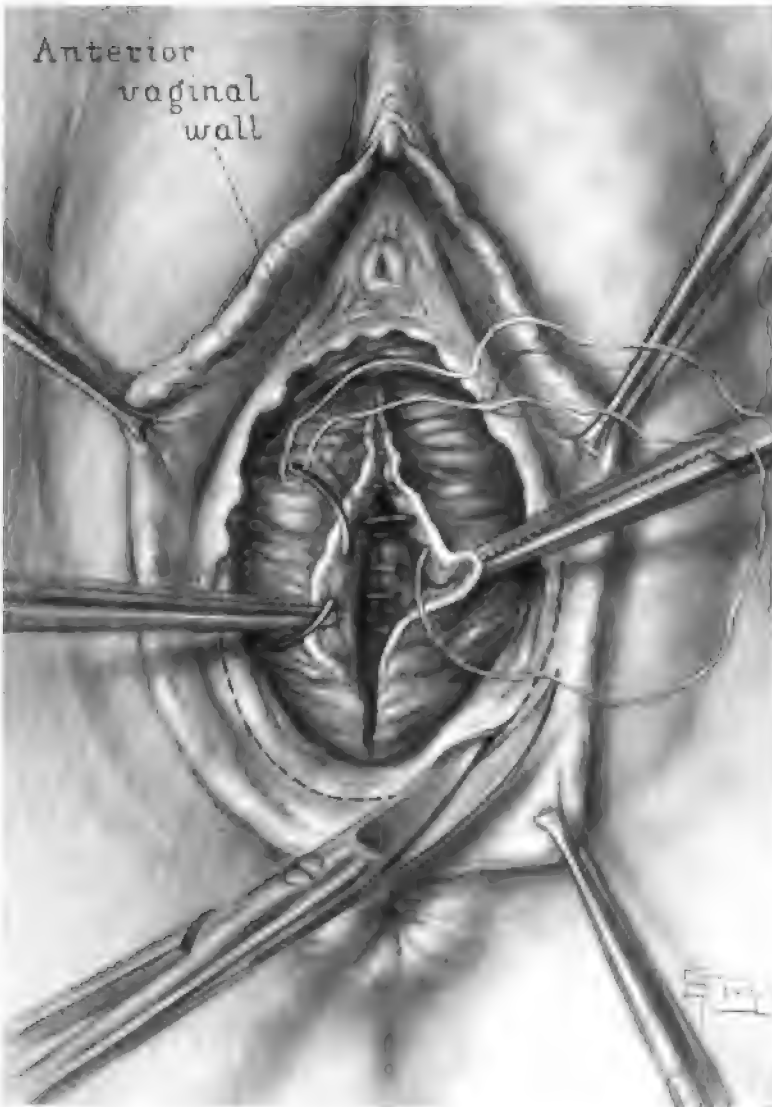
Fig. 153.—Incision of perineal region with closure of anterior vaginal wall.

ments.   The loose ends of the exposed broad ligament are now
approximated by a running buttonhole stitch extending back to
the perineal position and the sides of the vaginal mucosal flaps,
and closed by a running catgut suture in a submucous manner
(Fig. 153).   No sutures are exposed.   By such an operation one
secures all the advantages of the interposition operation without
the disadvantages of atrophying uterus and muscles which will not
support traction.   The complete elevation of the bladder is se-
cured, and it rests on the broad ligaments, which make a complete
transverse pelvic support.   Cystocele cannot form between the
pubic bones and broad ligaments because their position is secured
by suture.   Formerly the broad ligaments were passed by each
other, overlapping like a double-breasted coat, and two rows of
sutures were required.   The present method is somewhat more
simple, as effectual and safer, as no ends of vessels are left within
the pelvic peritoneum.   Perineal restoration is, of course, included
in all operations for prolapse.   These patients are usually confined
to bed ten days, and for a slightly longer period at the hospital.

DUCTLESS GLANDS

THE SURGICAL TREATMENT OF EXOPH-
THALMOS *

CHARLES H. MAYO

Exophthalmos of slight degree may occur in high degrees of
myopia, but when more marked it is commonly caused by the
growth of soft tissue or bony tumors in the back of the orbit, and
rarely it may be produced by arteriovenous aneurysm. The only
constitutional disease causing the condition is exophthalmic goiter.
The peculiar staring with widening of the palpebral fissure caused
by myocardial disease is often confused with exophthalmos. In
this way toxic goiter may be confused with true hyperthyroidism,
as pointed out by Plummer.[1]

Exophthalmic goiter was described by various observers in the
latter half of the eighteenth century, notably by Morgagni[2] and
Parry,[3] followed in the first half of the nineteenth century by further
writings of Parry, Flajani,[4] Graves,[5] Basedow,[6] and numerous
others. Each described the symptoms of hyperthyroidism with
sufficient accuracy to leave no doubt that their observations were
made on the same type of cases.

It was Graves, however, in his lectures in 1835, who laid the
most stress on exophthalmos. Many observers do not consider
the condition to be true Graves' disease unless the protrusion of the
eye is marked enough to be easily recognized. This was correct,
since early observers based their diagnoses on symptoms unsup-
ported by pathologic evidence. If the other symptoms were
present, it was considered pseudo-Graves' disease until exophthal-
mos occurred. Usually, however, the staring (of Stellwag) and the

widening of the palpebral fissure (of Dalrymple) were accepted in lieu of exophthalmos.

The eye symptoms in hyperthyroidism are so striking in character and often so distressing to the mind of the patient that they have been made the subject of frequent observation. In extreme cases, erosions and ulcers of the cornea occur. I have observed two patients totally blind from this cause, and several patients blind in one eye. The lagging behind of the lids, which follow the movement of the eyeball with a jerking motion, was noted by Graefe.[7] Stellwag[8] noted the staring without winking for much longer intervals than common. Dalrymple[9] noted the unnatural widening of the palpebral fissure, and Möbius[10] observed that when exophthalmos was extremely marked, diplopia occurred on near vision. The exophthalmos was ordinarily considered a congestion of the venous plexus of vessels at the back of the orbit and therefore connected with the circulatory disturbance of the disease.

The late Dr. Landström,[11] of Stockholm, has given a most acceptable version of the development of exophthalmos in hyperthyroidism. He has shown that a previously undescribed microscopic muscle in streaked layers occurs in the fascia behind the eyeball and about the globe.

This irregular muscular sheath is attached forward to the lids and anterior orbital fascia. The muscle bundles are irregularly placed and are scarcely to be distinguished macroscopically, but may readily be found microscopically. They are under the control of the sympathetic nervous system and their function is to resist the action of the four active orbital muscles which otherwise draw the eyeball back. When irritated, they draw the eyeball forward and the lids backward. This muscular system is additional to the well-known muscle of Müller.[12]

It was noted in 1873 that the irritation of the sympathetic ganglion caused dilatation of the iris with some protrusion of the globe. The experiments of Bénard[13] confirmed these observations and showed that, by the irritation of the cervical sympathetic, the eyeball is pressed forward and to a certain degree the closure of the eyelids is prevented. It is therefore doubtless the

sympathetic which innervates these muscles, and an irritation of its fibers doubtless affects this muscle first, the symptoms observed by Stellwag, Graefe and Dalrymple being produced as a direct result of such irritation.

Wiener[14] showed that irritation of the sympathetic ganglion caused increased intra-ocular tension, while its destruction caused lower tension for a time.   This led to the operations on the sympathetic for the cure of glaucoma by lowering the tension and causing contraction of the iris.

Trousseau[15] believed the cervical sympathetic to be involved in exophthalmic goiter, and an operation which would relieve this extremely marked feature of the disease was looked on by him as being at least theoretically advisable.

Jaboulay,[16] in 1896, was the first to introduce an operation on the sympathetic ganglion for exophthalmic goiter. His most enthusiastic disciples were Abadie and Jonnesco.   While quite a number of operations on the cervical sympathetic for hyperthyroidism have been performed at a few clinics, especially Jonnesco's, and a few scattered operations have been performed at many clinics, the relief in general is apparently about the same as that which follows ligation of the vessels and injection of boiling water into the gland.   The reduction of the exophthalmos is often very marked.

In 1906, before a meeting of French surgeons, Abadie[17] stated that this operation produced perfect cures, while partial extirpation of the thyroid removed only part of the symptoms, and did uot remove the exophthalmos.   He maintained that sympathectomy would surely cause the disappearance of the exophthalmos.

Balacescu[18] believes that the removal of the whole of the cervical sympathetic is indicated and that no bad results follow the operation.

It is very certain that while the surgical ablation of the greater part of the thyroid cures in the majority of cases of hyperthyroidism, and even relieves eye-symptoms in most cases, yet in numerous instances this one feature remains to distress the patients when otherwise they feel very well.

Some of these patients are greatly improved by a secondary
        '14—22

operation which consists of scalping the edge of both lids from a
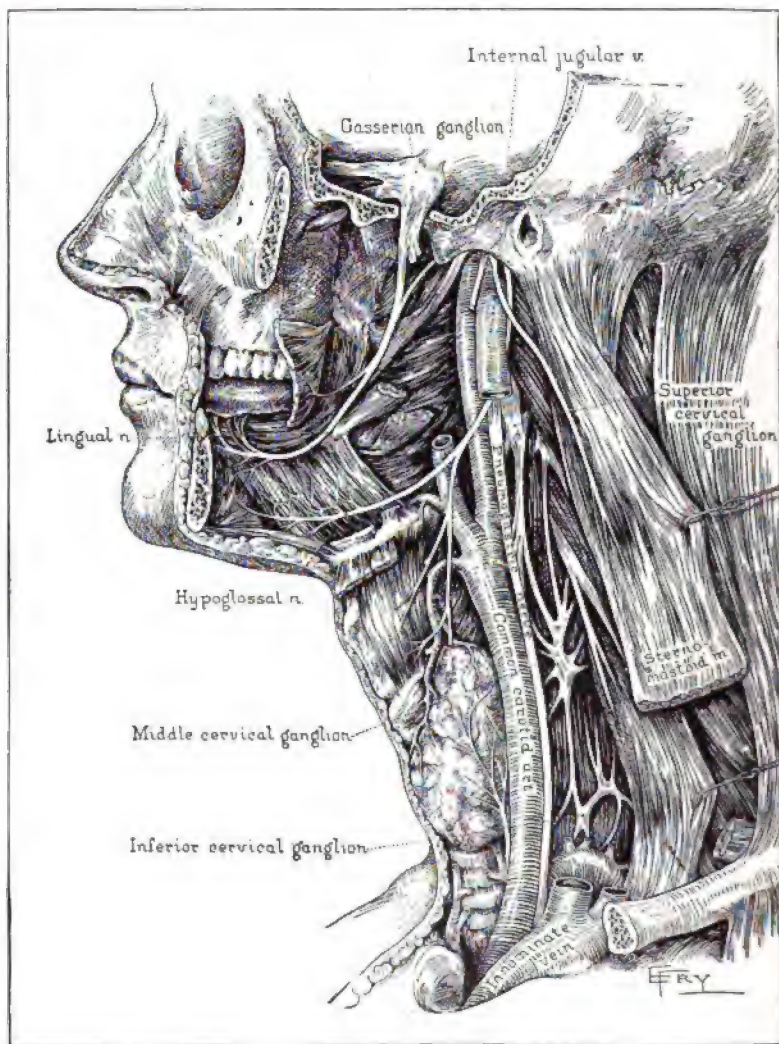
Fig. 154.—Showing position of superior, middle, and inferior cervical ganglions.

quarter to a third of an inch at the outer canthus and uniting the
margins of the lid.   The Jaboulay operation, that is, a cervical

sympathectomy of the superior and sometimes of the middle ganglia (Fig. 154) for the purpose of reducing exophthalmos and securing a slight ptosis of the upper lids has been used in our clinic. In cases of hyperthyroidism in which the exophthalmos is extreme and the nervous symptoms out of proportion to the size of the thyroid, the sympathetic ganglia are removed and in the same
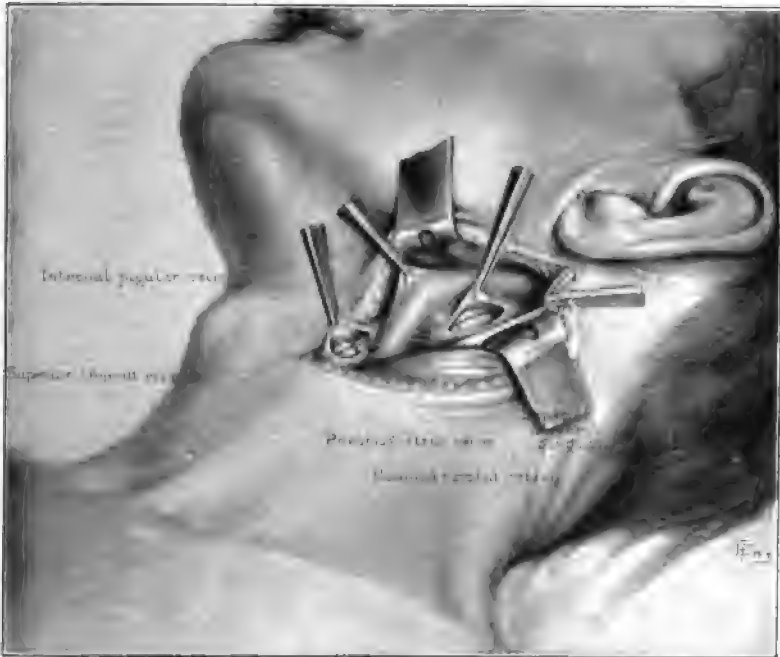
Fig. 155.—Shows incision into the sheath of the carotid vessels and exposure of pneumogastric nerve. Dissection of superior cervical ganglion and superior thyroid vessels ligated.

incision the superior thyroid vessels are ligated. This operation can be done with novocain as a local anesthetic, but is preferably made with a general or combined anesthetic. Incisions are made in the lines of the natural creases in the neck opposite the bifurcation of the carotid (Fig. 155). The sternomastoid is drawn outward and a blunt dissection is made down to the jugular and carotid veins, which are then drawn inward. The posterior sheath of

fascia inclosing these vessels is opened that the vagus nerve may be kept under observation, since this nerve is bulbous above this point and might be confused with the sympathetic.

Under normal conditions the sympathetic ganglion is $\frac{1}{8}$ to $\frac{1}{4}$ inch wide. Many branches lead from it on either side. The connecting branches are divided, the upper part of the ganglion torn off or cut and the lower portions of the nerve cut or torn off at the middle ganglion unless the middle ganglion is also removed. The wound is closed without drainage.

When the sympathetic ganglion is thus removed with the middle cervical ganglion, the result is very good in securing relaxation of the eyeball and slight ptosis of the upper lid, with great general improvement of symptoms. In some cases in which the sympathetic does not seem to occur as a ganglion, but in which fewer and larger communicating branches are found, the result has not been so good, some patients receiving but slight benefit from the operation, the operation seemingly being incomplete. The ease with which it is performed and the excellent results which frequently follow its employment, however, warrant its consideration for the relief of certain patients suffering from extreme degrees of exophthalmos.

In our cases in which the vessels of both upper poles were ligated in addition to the sympathectomy the primary results were good, but the time since operation is yet too short to warrant a positive statement as to the permanency of cure. Time will show just how extensive resections of the sympathetic may be made without causing complications.

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HYPERTHYROIDISM: PRIMARY AND LATE RESULTS OF OPERATION *

CHARLES H. MAYO

The term hyperthyroidism is expressive of a group of symptoms, the symptom-complex of which has been seen and described under various names in all countries.

The thyroid is necessary in the growth and development of body and brain, and must also be classified among both the glands of nutrition and glands of defense. Like all essential organs and kinetic glands of the body, it has a wide variation of its activity within the limits of health. Probably the secretion of one-sixth of the adult gland is enough to maintain the metabolic balance, which is no more surprising than that one-half of one kidney will maintain urinary balance. A similar condition exists in many of the other organs of the body.

There are many factors which control such organs, yet any or all of them may be temporarily deficient or overactive in their functions; but unless there be an actual great loss of cells or a markedly hyperplastic condition, they are held in control. In this variation of activity in the normal thyroid and in the normal changes in activity of its various vesicles the thyroid sometimes manifests a storage function, retaining for a time its secretion and depositing colloid substance for this purpose. This automatic adjustment of function of the glands, both duct and ductless, explains why so futile is the effort to transplant glands from other animals to the human, with the expectation that the gland will auto-

matically functionate.   Especially is this true of the reported cases
of the transplantation of glands from animal to man in which there
is always a definite laking of the blood.   A temporary benefit may
be obtained, however, from the transplantation of the glands of
internal secretion through the digestive power of the phagocytes.

That there should be a definite microscopic picture in so definite
a disease as hyperthyroidism is to be expected.   The only organ
that gives such an exclusive picture is the thyroid.   The trained
pathologist should not only recognize the condition, but also its
degree of activity and its stages; that is, whether progressing,
regressing, or regenerating.   In the pathologic examination the
whole of the tissue removed must be macroscopically observed,
that an unessentially small area of hyperplasia or of colloid storage
be not chosen as the sole picture of the glandular histology.   The
changes in so small an amount of tissue may be neutralized by
other factors.   The pathologic material from our cases has been
studied by Wilson.*

It is possible that overactivity of the thyroid may arise from
extra demands made upon the gland in its capacity for nutrition
or defense in toxic conditions. . Possibly in its latent sex relation-
ship such demands may be temporary or long continued.   For a
time the excess secretion may be neutralized.   When shock is
attributed as the cause of sudden onset of hyperthyroidism, it is
often only an evidence that the equilibrium of the nervous system
has been upset in the presence of a latent hyperplastic thyroid,
thus producing the sudden symptoms which had previously been
controlled or neutralized.

Up to July 1, 1914, 6960 operations had been performed for
goiter in our clinic.   Of these, 3327 were performed upon patients
with hyperthyroidism.   The greater number of these patients
have been seen clinically by Plummer.†

The various types of goiter should be treated both medically
and surgically.   Many goiters of the simple and mild exophthalmic
types undoubtedly regress spontaneously, although various forms

* Collected Papers, 1913, 539–543 and 544–553.
† Collected Papers, 1913, 447–454 and 455–460.

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of medical treatment may hasten the recovery and restoration of the gland to an apparently normal condition in many instances, especially in the early stages of simple goiter.

Exophthalmic goiter is essentially a disease of a chronic character, presenting exacerbations and ameliorations of symptoms extending over a period of months or several years. After the first year a gland often undergoes a regression.

While exophthalmic goiter is amenable to surgical treatment by the removal of a large amount of the hypersecreting gland, it is by no means urgent surgery that is required, and all patients during periods of exacerbation should be considered as medical cases. Surgery is indicated in the upwave of improvement. However, the majority of these cases can withstand thyroidectomy at the time they are seen by the surgeon. Extreme conditions, especially dilatation of the heart, may require medical preparation, and the operative interference following in cases resistant to treatment may be confined to injections of boiling water into the gland, after Porter's plan, to hasten improvement. In most of the severe cases the ligation of the right upper pole is indicated a week later, and thyroidectomy reserved until about four months have elapsed, by which time these patients will usually have made an average gain of about 22 pounds, with great general improvement. However, if the reaction following the left ligation is not unduly severe, a partial thyroidectomy may be made at the second operation the week following.

The great lowering of mortality following operation for exophthalmic goiter is due less to trivial details of technic than to the better judgment in the preparation of patients, the selection of a time, type, and extent of operation, and its division into stages, with varying intervals of rest. The high mortality of the past is no longer a determining factor against the surgical treatment. As many as 278 consecutive operations have been made on the thyroid between deaths occurring from the operation. The average operative mortality at present probably varies from 1 to 3 per cent. Relapse of some degree occurs in a small percentage of cases

through the removal of too small an amount of the thyroid. Such cases should be reoperated on.

It may be well to note here the effect of pregnancy during the progress of the disease or following the operation. A few of these patients are in much better health during pregnancy; however, in the majority the symptoms are worse. I believe that the risk to life incident to pregnancy and labor is less than from abortion, which rarely should be produced, since most of these patients improve after childbirth.

STUDIES IN THE CHEMISTRY AND PHYSIOLOGY OF THE THYROID

I. THE DETERMINATION OF IODIN IN THE THYROID *

EDWARD C. KENDALL

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In July, 1912, I published an article on the determination of iodin in the presence of chlorids, bromids, and organic matter. Since that time the method has been in almost constant use for the estimation of iodin in connection with studies in thyroid activity. As several inquiries concerning the method have been received, and as some of the details have been modified, it seems desirable at the present time to describe the method with the modifications which have resulted from several hundred determinations of iodin.

The chemical reactions upon which the method is based are described in the original article and will not be given here. The determination of iodin, when present in amounts ranging from 0.005 to 5 mgm., is as follows:

The first step is the destruction of organic matter and the retention of the iodin as sodium iodid. This is accomplished by fusion with sodium hydroxid in a nickel crucible. In order to maintain a proper degree of temperature and to prevent loss of iodin by volatilization the crucible is heated indirectly by placing inside a larger crucible the bottom of which is covered with a layer of sand 0.5, cm. in thickness (Fig. 156). The drawing shows in detail the construction of the heating apparatus. The support-
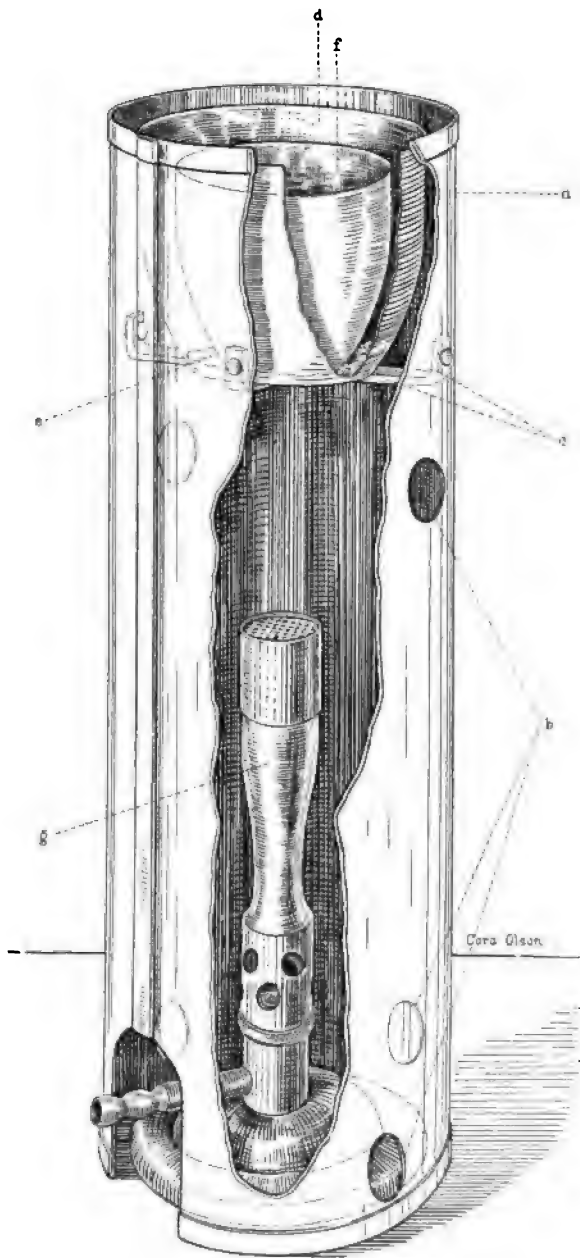
Fig. 156.—*a*, Supporting cylinder of sheet iron; *b*, holes to supply air to burner; *c*, cross-bars for supporting large crucible; *d*, large crucible, 7.8 cm. in diameter; *e*, 0.5 cm. of sand on bottom of large crucible; *f*, fusion crucible, 5.9 cm. in diameter; *g*, No. 3 Meker burner.

ing cylinder is 9.4 cm. in diameter and 30 cm. high; the cross-bars which support the large crucible are 7.5 cm. from the top. Both crucibles are of pure nickel, the larger one 7.8 cm., and the smaller one 5.9 cm., in diameter. The burner is preferably a 15.6 cm. (No. 3) Meker burner.

For the determination of iodin in thyroid preparations the most satisfactory weight of the material to be analyzed is 0.5 gram. Whether this is in the form of a dry powder, a solution, or a moist precipitate on a filter-paper, the same procedure is carried out. The material is placed in a 5.9 cm. nickel crucible and moistened with 5 to 6 c.c. of 30 per cent. sodium hydroxid; 10 to 15 grams of stick sodium hydroxid which has been broken into small pieces are added, and the crucible placed on a hot plate until the excess of water is evaporated and the contents have a thick, syrupy consistence. If but little organic matter is present, there is a tendency for spattering of fine drops during the evaporation of the excess water. If some organic substance is dissolved in the solution, this spattering is prevented. A small amount of gallic acid is suitable and sufficient for this purpose.

For the fusion of the organic matter with the sodium hydroxid, it is necessary to heat the bottom of the large crucible to a dull red heat. If the crucible is heated too much, the fusion in the small crucible will creep up the sides and sodium hydroxid will volatilize, with loss of iodin. If the large crucible is not heated sufficiently, the destruction of organic matter will not be complete. However, there is a wide range of temperature between the two limits, and after a little experience no difficulty is encountered.

When the sodium hydroxid is first heated in the presence of water, considerable foaming is produced. This, however, does not extend to more than half way up the sides of the crucible. As the heating continues the foaming becomes less, and after five to ten minutes the melt settles to the bottom. Bubbles will continue to be given off for some time (five minutes or so), depending upon the nature of the organic matter.

When the melt has settled to the bottom and only a few bubbles of gas are being liberated, the small crucible is removed with

crucible tongs, and partially cooled by agitating the contents with a rotary motion. This will also remelt and carry to the bottom any particles of the fusion which have solidified on the cooler sides of the crucible.

Five to 10 mgm. of potassium nitrate are now added. This will oxidize the remaining organic matter and cause a liberation of bubbles. If only a few bubbles are liberated, a second addition of 5 to 10 mgm. of potassium nitrate will not cause a further liberation of bubbles, and the oxidation of the organic matter is complete. If the second addition of nitrate causes a further oxidation, repeated additions of 5 to 10 mgm. of the nitrate are made until no more bubbles of gas are produced by the addition of the nitrate. The melt is now poured into the shallow cover of the 5.9 cm. crucible and allowed to cool.

The entire time required for the fusion is ten to fifteen minutes. I find it most convenient to use two crucible-supporting cylinders and to carry on two fusions at the same time.

When the melt and crucible are cool, they are placed in a tall beaker of from 600 to 800 c.c. capacity, together with a little talcum powder and 125 to 150 c.c. of water. The beaker is placed on a hot plate. After the melt is dissolved, it is transferred to a 500 c.c. Erlenmeyer flask. It should be a colorless, clear solution with a volume of about 200 c.c. To the solution 1 c.c. of 10 per cent. of sodium bisulphite* and a few drops of methyl-orange are added. The solution is cooled by immersing the flask in cold running water. When cool, 85 per cent. phosphoric acid is added by allowing the acid to run directly into the flask from a pipet or siphon having a small delivery tube. The flask is vigorously and constantly shaken with a rotary motion to expel the carbon dioxid. As the indicator begins to turn pink the neutralization is finished slowly, so that only a few drops are added after the

* The bisulphite is added to supply a reducing action to the solution which prevents the loss of iodin. As the iodin is kept in the form of hydriodic acid, no loss can occur. More than 1 c.c. of bisulphite should not be added, as it produces hydrobromic acid from the bromin and this in excess reduces iodic acid, giving low results.

indicator has changed. This is a very important condition to satisfy, as too much acid will cause low results. A few drops of bromin are now added, and the solution shaken until the bromin colors the solution a distinct yellow. This is essential, as the addition of too little bromin will prevent the subsequent determination of the iodin.

The volume of the solution should be made between 250 and 300 c.c. The flask is placed on the hot plate and boiled from eight to ten minutes. The talcum powder causes a rapid boiling and the bromin is quickly expelled. When the solution becomes colorless,* the flask is removed from the hot plate, five to ten drops of 5 per cent. solution of sodium salicylate† are added, and the flask is immersed in cold water. The volume of the solution after boiling should not be less than 175 to 200 c.c., as the high concentration of the salts makes the end point less sharply defined if the solution is boiled down to a small volume.‡

When the solution is cool, 5 c.c. of 10 per cent. potassium iodid are added. If there is not an immediate liberation of iodin, 3 to 4 c.c. of 85 per cent. phosphoric acid are added.§

The liberated iodin is now titrated with $\frac{N}{200}$ sodium thiosulphate.‖ The titration is finished with aid of the blue starch-

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* The bromin destroys the color of the methyl-orange.

† This is best prepared by dissolving 5 grams of pure salicylic acid in dilute sodium hydroxid and diluting to 100 c.c. The solution should be only slightly alkaline.

‡ Experience has shown that practically all samples of distilled water will take up small amounts of iodin. As this reducing action is destroyed by boiling with bromin, this source of error is entirely controlled under the conditions of the method as described above. However, a considerable error may result in the determination of iodin if any distilled water is added after the bromin has been boiled out of solution.

§ The acid is added after boiling out the bromin rather than before, at the acidification of the fusion melt, as low results may occur when the solution is boiled in the presence of a large excess of phosphoric acid. No error is caused by adding even a large excess of the acid to the cold solution.

‖ The most convenient strength of sodium thiosulphate for amounts of iodin ranging from 0.5 to 5 mgm. is 0.005 N. This is not a stable solution, and must be frequently restandardized. A convenient method proposed by Hunter is to prepare a solution of potassium acid iodate, which is equivalent to a known weight of iodin. The strength of any sample of thiosulphate is readily found by titrating the iodin liberated by the acid iodate solution, which retains its strength indefinitely. The iodin equivalent of the potassium iodate is found as follows: Prepare an 0.1 N solution of potassium acid iodate, KIO_3HIO_3, by dissolving 3.249 grams of the

iodin color.   For this, 0.5 per cent. solution of Kahlbaum's soluble starch is recommended.

In my opinion the most convenient procedure, where a number of determinations are made each day, is to use six or seven crucibles, each marked with a letter for identification.   Each crucible has a corresponding 500 c.c. Erlenmeyer flask marked with the same letter.   The crucibles are used in rotation.

The methyl-orange, bromin, and sodium salicylate are kept in dropping bottles.   The sodium bisulphite is kept in a 500 c.c. bottle fitted with a graduated pipet which passes through the cork and reaches to the bottom of the bottle.   The 85 per cent. phosphoric acid, the 10 per cent. potassium iodid, and the starch solution are kept in bottles fitted with siphons.   This form of container prevents contamination and offers a convenient means of supply for the respective solutions.

In regard to the accuracy and limitations of the method, the results of over 2000 determinations of iodin show that the method will detect as little as 0.005 mgm. of iodin.   One great advantage of the method is the entire absence of any test for iodin in cases where there is no iodin present.

Where iodin ranges from 1 to 5 mgm., duplicate determinations should not differ more than 0.01 to 0.02 mgm., which means a difference in buret readings of but 0.1 to 0.2 cubic centimeter.

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salt in 1 liter of water. This solution, diluted 20 times, will be approximately 0.005 N.   Dissolve a known weight of pure iodin (approximately 1 gram) in 1 liter of water containing 5 to 6 grams of sodium hydroxid.   Dilute this 10 times.   One cubic centimeter of this solution will contain 0.1 mgm. of iodin.   Measure 25 c.c. of this solution into a 500 c.c. flask, and dilute to 200 c.c.; add 5 to 10 drops 85 per cent. phosphoric acid and a few drops of bromin; boil out the bromin; add 5 to 10 drops of 5 per cent. sodium salicylate, cool, add 5 to 10 grams of sodium chlorid, then add 5 c.c. 10 per cent. potassium iodin, and titrate the liberated iodin with approximately 0.005 N thiosulphate.   This will establish the relation between "original iodin" and the 0.005 N thiosulphate, and from this the iodin equivalent of the potassium acid iodate can be found by adding a known volume of the acid iodate to 150 c.c of water containing potassium iodid, and 5 drops of 85 per cent. phosphoric acid and 5 to 10 grams of sodium chlorid.   When a small amount of iodic acid is in a solution which contains but a small amount of salts, the reaction with potassium iodid is retarded and the end point of the titration with thiosulphate is uncertain.   The addition of 5 to 10 grams of sodium chlorid to such a solution accelerates the liberation of iodin and makes the end point sharp and accurate.   The sodium chlorid must not be added until *after* the solution has been boiled with bromin.

II. A METHOD OF DECOMPOSITION OF THE PRO-
TEINS OF THE THYROID, WITH A DESCRIPTION
OF CERTAIN CONSTITUENTS*

In 1895 Baumann[1] reported the discovery of iodin in the thy-
roid, and during the succeeding years there has been an ever-
increasing interest in the study of the chemical constituents and
physiologic activity of the gland. As early as 1896 Gottlieb[2]
made the statement that, from clinical and experimental observa-
tions, it is evident that there must be more than one physiologically
active compound in the thyroid, but up to the present time no
compound of known chemical constitution has been isolated which
produces physiologic effects similar to those of desiccated thyroid.
Attempts to isolate the active principle have resulted in prepara-
tions which may be divided into two classes: First, those secured
by separation of products of protein nature without decomposition
or destruction of the protein molecule, and, second, those obtained
by means of hydrolysis of the protein and the subsequent separation
of the decomposition products. In the first class of preparations
are Oswald's[3] thyro-globulin and iodin-free nucleoprotein. Other
investigators have prepared similar proteins from the thyroid.
These products, which are original protein compounds unchanged
in chemical nature, still retain their activity, as shown in the treat-
ment of symptoms of cretinism and myxedema. In the second
class of preparations Baumann's[1] iodothyrin, containing about 9
per cent. of iodin, is the result of the decomposition of the proteins
with sulphuric acid. The iodothyrin so obtained is about 4 per
cent. of the total weight of the dried thyroid. It has some physi-
ologic activity, but the original claim of Baumann that it is *the*
physiologically active principle of the thyroid has long since been
disproved.

Other decomposition products have been obtained by Hutchison,[4] working with pepsin and trypsin on the thyroid proteins. Hutchison[4] separated in this way a product containing 3.4 per cent. of iodin.

Another means of throwing light on the nature of the iodin compound has been to prepare various iodin compounds and test the physiologic activity of these. Di-iodotyrosin, tetra-iodohistidin, tri-iodo-imidazol, iodized tryptophan and iodized phenylalanin, and other organic compounds have been tested in this way,[5] but no compound has been found which produces effects similar to those of desiccated thyroid.

Four years ago I took up the investigation of the chemical constituents of the thyroid. The object of the work was to isolate in pure form one or more chemical compounds which possess physiologic activity. Dialysis was used as a preliminary study of the proteins of the gland and the nature of iodin combination. Desiccated thyroid, either in suspension or dissolved in dilute alkali, will lose less than 5 per cent. of its total iodin by dialysis in a collodion sac against running water. Experiments were then made varying the temperature and acidity of the dialysate. These results showed that increase in temperature and acidity favored dialysis of the iodin compound, and as much as 40 per cent. could be made to pass through the sac in this way. Attempts were then made to alter the nature of the proteins to see the attending influence on dialysis of the iodin. Boiling in strong sodium hydroxid allowed 80 per cent. of the iodin to pass the dialyzing sac. Boiling with sodium hydroxid and hydrogen peroxid allowed 94 per cent. to pass.

These results showed a decomposition of the protein and a probable splitting-off of iodin in the inorganic form. As such vigorous treatment would undoubtedly destroy physiologic activity, further experiments were carried out to find some treatment which would break down the complex proteins into simpler products without destruction of the compounds so obtained. Alcohol was tried as a medium for the carrying out of such treatment. Alcohol saturated with hydrochloric acid gas was tried as a hydrolytic agent, but no satisfactory cleavage resulted from its use. Hydrol-
'14—23

ysis with sodium hydroxid in alcohol was then tried, and it was found that this method produced a cleavage different from any of the others. Seventy-five per cent. of the iodin was dialyzable, but it was easily shown that the iodin was not split off as sodium iodid, but still existed in organic combination. After it was shown that sodium hydroxid in alcohol altered the nature of the protein to a marked degree, dialysis, as a criterion of the nature of the iodin combination, was discontinued, and a detailed study of the chemical properties of these products of hydrolysis was begun.

No specific precipitant was found for the iodin compound in either an alcoholic or aqueous solution. After many attempts to find such a reagent it became apparent that the iodin was present in two different forms of organic combination. About 50 per cent. of the total iodin was soluble in acid and 50 per cent. was insoluble. As the solubility in acids effected a separation between the two apparently different iodin compounds, this treatment was used as the first step in the separation of the products of hydrolysis. Those compounds insoluble in acid are designated constituents of Group "A," and those soluble, constituents of Group "B."

All the constituents of Group "B" are easily dialyzable. Saturation of a solution of "B" with ammonium sulphate produces a sticky, tarry precipitate which evidently consists of amino-acid complexes, and carries down with it about 80 per cent. of the iodin in "B," showing that it is still present in organic combination.

Among the constituents of "B" not precipitated with ammonium sulphate is a compound that reduces alkaline mercury and silver salts. Evaporation of the solution to dryness with sodium hydroxid does not affect its reducing power, hence the reduction of the silver cannot be due to ammonium compounds. This reducing compound has been designated "R."

The iodin compound in "B" is precipitated to a large extent with mercury sulphate, and almost quantitatively with silver sulphate in the presence of magnesium oxid. A large percentage of the iodin is split off by this treatment. Oxidizing agents, even copper acetate, also easily split off the iodin from its organic combination.

After establishing the general chemical properties of Group "B" efforts were directed to a more extended study of Group "A." The most striking chemical property of "A" is its acidic nature. All the constituents of "A" are easily soluble in dilute alkali or ammonia and are reprecipitated by any acid.

Experiments with organic solvents showed that uncombined sulphur, fatty acids, and about 10 per cent. of the iodin in "A" is soluble in ether. The fatty acids doubtless came from the fats which were saponified by the alkaline alcohol, and the sulphur probably resulted from the decomposition of cystin. Further experiments showed that the solubility of the iodin in organic solvents varies greatly, it being least soluble in petroleum ether. The second step, therefore, for the purification of "A", is the removal of fatty acids and sulphur by extraction with petroleum ether. The product thus obtained contains about 4 per cent. of iodin, and this preparation may be dissolved in alkali and reprecipitated with acids without appreciable loss of its total iodin. This treatment slowly removes some constituents containing nitrogen, but not iodin, so that the percentage of iodin in "A" may thus be increased to about 6 per cent.

This preparation is a dark-brown powder, insoluble in water and acids, easily soluble in dilute alkali and ammonia. Its alkaline solution is precipitated by copper hydroxid, and to a large extent by barium, calcium, and magnesium salts. It is almost entirely soluble in ethyl acetate, but by partial extraction with this solvent it is possible to separate "A" into two fractions. In the ethyl acetate soluble portion of "A" the percentage of iodin is increased to 13 or 14 per cent., but the ethyl acetate insoluble fraction contains only 1.5 per cent. iodin.

Except for the insolubility in ether, the general chemical properties of "A" closely resemble those of a fatty acid. Upon further hydrolysis of purified fatty-acid free "A" by means of sodium hydroxid and a high temperature it was found that lauric acid and tryptophan are split off.*

* The purification of "A" and the isolation of a crystalline compound containing 60 per cent. of iodin will be described in another paper.

Having separated the chemical constituents of the thyroid into several fractions which have different chemical properties, it seemed desirable to test the physiologic activity of these different products. These will be described in logical rather than chronologic order.

For the testing of thyroid activity there are two methods possible: First, by relieving symptoms of hypothyroidism, as found in myxedema and cretinism; second, by the production of symptoms of hyperthyroidism similar to those of exophthalmic goiter. Testing by the first method, it was found that "B" has a specific action on the skin. The dry, scaly skin was changed to a moist normal condition by the use of "B" alone. Also certain subjective symptoms were entirely relieved. These were soreness of bones and joints and heat flashes over the skin. Muscle cramps were relieved and prevented by the compound "R." When "B" was tested by the second method, it was found that no toxic symptoms could be produced by any of the constituents of "B." Many tests carried on over a long period have failed to produce any toxic effect from "B" given intravenously, subcutaneously, or by mouth.

Testing "A" by the first method, it was found that subnormal pulse and temperature were raised to normal, metabolism was increased, as shown by increase in nitrogen excretion and decrease in weight, and the mentality in cases of myxedema was brightened.

Testing "A" by the second method, toxic symptoms are produced by the administration of "A." When injected subcutaneously in animals, there is at first no effect on either the pulse-rate or the blood-pressure. After twenty-four to thirty-six hours the dog appears restless, has a slight increase in temperature, and a decided increase in pulse-rate. If a series of injections is given on successive days, these symptoms are aggravated, and after two or three injections they are accompanied by a distinct tremor, loss of weight, and severe diarrhea. On the fourth or fifth day of injection the pulse-rate is between 200 and 300, and all the other symptoms continue with increased severity. This condition is followed by a sudden drop in the pulse-rate, and continued injections at this time will not make the pulse-rate return to its former high level, although the nervousness and tremor, loss of weight, and diarrhea

continue without decrease in their severity.   The dog in this condition presents a picture very similar to that of exophthalmic goiter. If the injections are now discontinued, all symptoms rapidly disappear and the dog will return to its former weight.   The change in the pulse-rate is interesting at this time, as it not only returns to normal, but becomes much lower than before the injections had been given.   These experiments have been repeated many times, giving practically the same result, and show that "A" produces toxic symptoms similar to those of hyperthyroidism.

After it was found that the pulse-rate could not be maintained at a very high figure for more than a few days, although the injections were continued, the question arose as to whether or not the animal developed a tolerance for the compound acting on the heart. If an immunity did result, it should be able to counteract the effect of a second series of injections given immediately after the animal returned to normal.   To decide this question the animal was given a series of injections on several successive days, and after a marked toxic condition was obtained the animal was allowed to recover. After an interval of several days a second series of injections exactly similar to the first was given.   Under these conditions the nervousness, tremor, and diarrhea appeared to be about as severe, but the pulse-rate was much slower in responding to the injections, and at no time reached as high a figure as during the first series.   There was no sudden drop in the pulse-rate as before, and it did not return to normal for a longer period, the animal appearing to experience greater difficulty in throwing off the effect of the injections.   After another interval during which the animal returned to normal, except in weight, a third series of injections was given similar to the first and second.   All the symptoms were again produced, the animal losing weight very rapidly.   The pulse appeared to be but slightly increased, but the least excitement or exertion would send it up to 280 or 300.   The animal seemed to be even less capable of resisting the toxic effect than before.

From the results we may draw the conclusion that the toxic compound does not produce symptoms in a rapid and direct manner.   It requires several hours before any effect is noticeable and

the symptoms continue for some time after stopping the injections. There is apparently some form of tolerance established in regard to the effect on the heart, but long-continued injections slowly exhaust the body's resisting power.

Further experiments showed that, for the production of these toxic symptoms, it is necessary for the "A" injected to contain iodin, and the severity of the symptoms depends upon the amount of iodin injected. "B" iodin injected in equal amount produces no apparent effect and will not produce tolerance to a subsequent injection of "A" iodin. Iodin in the form of potassium iodid injected in amount five times that used for testing "A" produced no increase in the pulse-rate. "A" prepared from desiccated thyroid or colloid goiters low in iodin is physiologically inert.

DETAILS OF THE METHOD FOR ALKALINE HYDROLYSIS OF PROTEINS OF THE THYROID

The preparation of finely powdered desiccated thyroid, as fat free as possible, is added to 90 per cent. ethyl alcohol containing 1 per cent. of sodium hydroxid, in the proportions of 2.5 grams of thyroid per 100 c.c. of alcohol. The powder is insoluble and settles to the bottom of the container. The alcohol is now boiled for forty-eight hours under a reflex condenser. During the heating ammonia is given off, which amounts to about 8 per cent. of the total nitrogen. At the end of this time the alcohol has dissolved the greater part of the powder and has a dark-brown color.

The hot alcoholic solution is now filtered with suction. There is a sticky, tarry residue in the bottom of the flask, which contains about 9 per cent. of the total nitrogen, 80 per cent. of the total phosphorus, and 7 per cent. of the total iodin.

The alcohol solution is diluted with water until there is about 75 per cent. of alcohol present, and the sodium hydroxid is neutralized with carbon dioxid or sulphuric acid. If sulphuric acid is used, the alcohol is cooled until the sodium sulphate crystallizes out. This is filtered off, and the alcohol is then distilled off, leaving a water solution of the split products. If carbon dioxid is used, the alcohol is distilled immediately, as the sodium carbonate will not separate
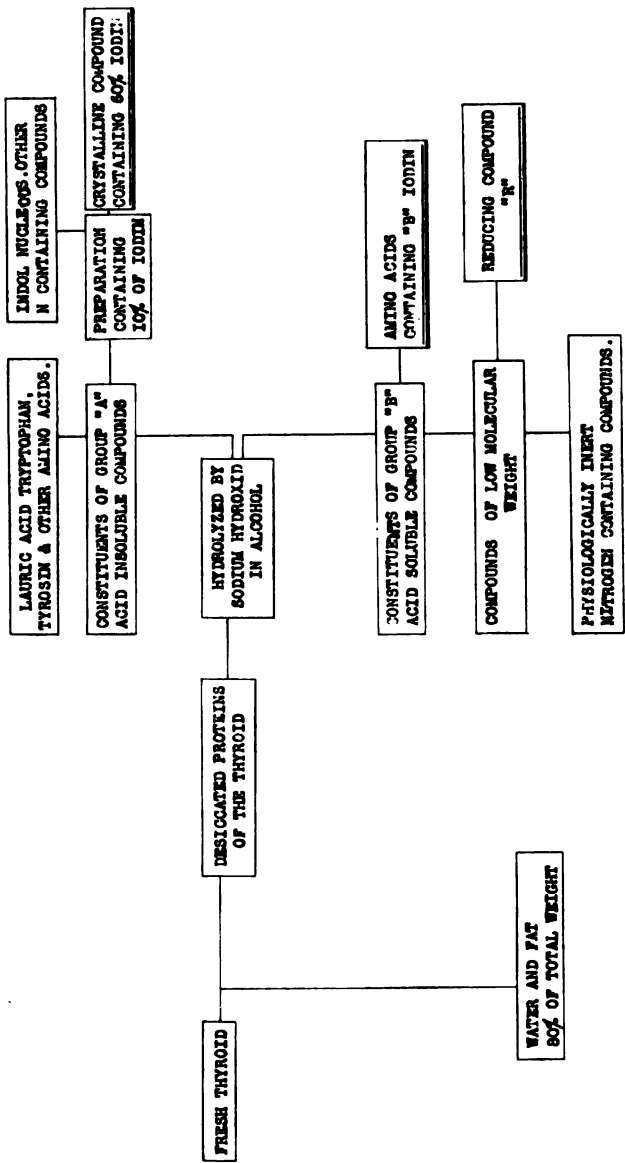
Fig. 157.—Chemical constituents of the thyroid.

satisfactorily.   The last traces of alcohol are removed by heating in an evaporating dish on the water-bath.   The water solution on cooling will solidify to a gelatinous mass if there is much fatty acid present.

The solution is diluted to about 100 c.c. for each 20 to 25 grams of original thyroid used, and is acidified with 20 per cent. sulphuric acid.   This produces a precipitate.   The acidification is continued until the addition of more acid ceases to cause a precipitate.

The solution is allowed to stand in the cold several hours—generally overnight.   The precipitate is filtered without suction and is washed with a little water.   This now is the first preparation of "A."   It is allowed to dry on absorbent paper and then is completely desiccated *in vacuo* over sulphuric acid.

The filtrate is "B."   It is neutralized with sodium carbonate evaporated to small volume, alcohol added, and the sodium sulphate crystallized out.   The alcohol is distilled off, and the resulting solution either desiccated or sterilized for therapeutic use. Fifteen to 20 per cent. alcohol may be used as a preservative.

The dry "A" is extracted with petroleum ether dissolved in dilute sodium hydroxid and reprecipitated with sulphuric acid. By warming the solution, after addition of the acid, to 60° or 70° F. and then cooling to 10° or 15°, the precipitate changes to a sandy, finely divided form, easily filtered.   "A" in this form is fat free, and amounts to about 5 per cent. of the total weight of thyroid taken.   Its percentage of iodin is about 10 times as much as that of the starting material, and for normal glands is equal to about 50 per cent. of the total iodin.

The distribution of nitrogen is as follows:

"B" contains 74 per cent. of the total nitrogen.
"A" contains 9 per cent. of the total nitrogen.
Alcohol residue contains 9 per cent. of the total nitrogen.
Liberated ammonia contains 8 per cent. of the total nitrogen.

(See Figs. 157 and 158.)

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Production of Hyperthyroid symptoms
in man and dogs.

No effect

No effect

Very rapid pulse

Nervousness

Nausea

Diarrhoea

Loss of weight

Severe headaches

"B"

"A"

Desiccated Thyroid

"B"

"A"

Symptoms of hypothyroidism
Myxoedema and Cretinism.

Dry scaly skin   Relieved by

Soreness of   Relieved by
bones and joints

Muscle cramps   Relieved by

Low pulse rate   Raised to normal by

Subnormal   Raised to normal by
temperature

Increase in weight   Relieved by
with oedema

                       Brightened by
Decrease in
mentality

Fig. 158.—Relation between physiologic activity and chemical constituents of the thyroid.

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THE THYROID AND A SUMMARY OF OUR PRESENT KNOWLEDGE OF GOITER *

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This thesis is an attempt to summarize our present knowledge of the physiology, pathology, symptomatology, and surgical treatment of the various forms of enlargement of the thyroid which are ordinarily grouped under the term goiter. Probably the diseases of no other important gland of the body, so long after their first recognition, have remained in such obscurity as have those associated with thyroid enlargement. The brilliant results of the empiric treatment of these diseases in recent years have focused thereon the attention of the medical world. This is perhaps sufficient reason for the present review.

Function.—The function of the thyroid in the human being is problematic. It has long been known that the gland is absolutely necessary to normal metabolism, and that its rôle is probably dependent on an internal secretion, yet, in spite of extensive experimentation, the true active principle in this internal secretion is still unknown. Neither has its method of action been discovered. Thus far our knowledge is practically limited to the fact that iodin in various combinations, particularly thyroidin, discovered by Baumann[1] in 1895, is an essential to the thyroid, but as yet no chemically pure substance which retains its physiologic activity has been isolated. The gland is indispensable to the maintenance of healthy life, and in order to explain its function, innumerable experiments have been made and many theories advanced, but all such theories are still conjectural. Notkin[2] believes that in the

thyroid a process of digestion takes place by which harmful products of metabolism are split up by an enzyme into useful and necessary substances. Another theory is that the gland is a secreting organ, actually affording nourishment to the body. Perhaps the most acceptable supposition is that the thyroid secretion neutralizes some toxic product of metabolism present in the blood, which otherwise would be harmful to the individual. Richardson[3] suggests that the function of the thyroid is probably associated with the exchange of respiratory gases between the blood and tissues. The supporting evidence for all these theories is insufficient, and is based on indirect deduction from experiments which demonstrate the rôle of thyroid tissue in abnormal dosage and under abnormal conditions. An investigator, in advancing his own ideas, can find much to disprove by experimentation in any and all other theories. To this is partly due the wide variance of published results of researches along similar lines in the hands of different men, and resulting in such a mass of confusing and contradictory detail as is found in the literature of the thyroid.

. That the thyroid has periods of normal physiologic activity is proved by its changes during the sexual life of the female. In the human being its enlargement during puberty, especially at each menstrual epoch, and its increase in size during pregnancy, are common observations. Animal experimentation shows that impregnation occurring in a thyroidectomized cat is likely to be followed by renal insufficiency and albuminuria. It is now believed that the development of eclampsia in woman bears a definite relationship to deficiency of thyroid secretion. The vomiting of pregnancy has often been completely relieved by the administration of small doses of thyroid after all other measures have failed.

As a ductless gland, the thyroid undoubtedly plays a part in the correlation of the internal secretions of the adrenals, pituitary, thymus, etc. There is sufficient evidence to prove that a close association exists, but further study is needed to show the exact physiology of the entire system of ductless glands. That each of these glands contains a hormone or hormones which act as a stimu-

lant to the performance of its own function and to counterbalance
the activity of some one of the other ductless glands is more than
a hypothesis in the light of recent research.   The works of Biedl[4]
and Falta[5] are complete in their compilation of our present knowl-
edge in reference to the ductless gland system.

One cannot justly leave the subject of the function of the
thyroid without some reference to the parathyroidal glandules.
Here again exact knowledge is limited to the general evidence that
the parathyroids are "functionating anatomic structures concerned
in body metabolism."   It is believed by many observers that in the
human being, at least, the importance of the parathyroids in their
actual association with the thyroid is overestimated.   Other ob-
servers even believe that the only relationship they bear to the
thyroid is topographic.   This, however, is an extreme view, and
an intermediate position probably will be proved ultimately.

Diseases.—In considering the diseases of the thyroid I shall
intentionally omit the rarer conditions of thyroiditis, tuberculosis,
syphilis, carcinoma, and sarcoma.   For convenience, all other
pathologic changes in the thyroid will be included under the term
goiter.

The clinical classification of goiter is still an unsettled question,
and I shall make use of what we believe to be the most practical
grouping, that proposed by Plummer,[6] and which embraces all
goiters.   He has divided goiters according to our present concep-
tion of their clinical and pathologic relationship into four groups:
(I) Non-hyperplastic atoxic;   (II) non-hyperplastic toxic;   (III)
hyperplastic atoxic;   (IV) hyperplastic toxic.   ·

GROUP I.—*Non-hyperplastic Atoxic.*—Under this heading are
considered all the so-called "simple" goiters, associated with which
the individual exhibits no evidence of any constitutional symptoms
that can in any way be attributable to the thyroid.   In North
America enlargement of the thyroid in the human being does not
occur endemically to any appreciable extent, neither have any epi-
demics appeared similar to those which have been reported in
foreign countries.   Goiter in the human being is more or less
evenly distributed over this continent, although in isolated villages

or small sections there may be a larger percentage of the population goitrous than the average throughout the country.

In patients with goiter who have come to our clinic a careful routine inquiry into the environment of the individuals, particularly with reference to the water-supply during their entire lives, and the compilation of the data therefrom, has never suggested any relationship to water as an etiologic factor in the production of the disease. Nevertheless, as implied, conditions are entirely different in North America from those existing in Europe. The Swiss Alps afford the most typical example of endemic goiter. For example, in a period of six years no less than 12,277 men were prevented from entering the Swiss army on account of goiter. In Italy the situation is similar, and, therefore, researches conducted in these regions of endemic goiter have been more productive than any in this country. But from the wealth of these investigations one is unable to prove more than what is quite apparent, that is, that, on the continent, goitrous districts are definite. Many theories have been advanced to explain this geographic distribution. The researches of Bircher[7] in Swiss goitrous districts were accepted as proving that, at least in certain localities, endemic goiter is due to a water-borne agent. During the past year, however, the studies of Dieterle, Hirschfeld, and Klinger[8] indicate that the goiters in the very regions in which Bircher conducted his experiments are entirely independent of rock, soil, or water-supply. The change taking place in these goiters after an alteration in the source of their water-supply they attribute to hygienic reforms and better sanitation, rather than to altered geologic factors. For a summary of the question of endemic goiter we owe much to the work of McCarrison,[9] who, in a recent monograph, gives the results of his investigations. He believes that the etiologic factor of endemic goiter is infection from the gastro-intestinal tract, and that there is a specific toxic agent in the production of this type of goiter, although he has not as yet obtained it. He has been able to cause goiters to disappear entirely by the use of vaccines prepared from the normal organisms inhabiting the bowel. In this country the work of Marine[10]

is the most noteworthy in the rôle of investigating the etiology of endemic goiter. McCarrison's hypothesis is supported by Sir Arbuthnot Lane,[11] who believes that goiter, both simple and exophthalmic, has been cured by short-circuiting the large bowel.

Pathology.—It is difficult to classify with any simplicity the various changes which are found in enlarged thyroids which are not associated with symptoms of disturbed function. It is accepted in our clinic that the non-toxic goiter is one in which there is no evidence of an epithelial hyperplasia or hypertrophy sufficient to characterize the gland. These simple enlargements of the thyroid may, therefore, be conveniently divided into two groups— (*a*) symmetric or thyroidal-shaped goiters; (*b*) asymmetric or nodular goiters (MacCarty).[12]   In the first group the diffuse hypertrophic colloid is the most typical and frequent, and is seen chiefly in the young individual. That this type of gland may undergo cellular hyperplasia and produce constitutional symptoms is recognized. Between this glandular hypertrophy and the typical hyperplastic thyroid every possible pathologic picture may be presented, which explains the confusion existing in classifying these changes. The second group, or the asymmetric enlargements, are practically always due to single or multiple adenomas. The essential pathology of many of the atoxic goiters examined in our clinic is confined to the presence of a single cystadenoma. In 45 per cent., however, the increase in size is due to multiple adenomas of various types.[13]   These are seldom confined to one lobe, although, as a rule, one lobe, usually the right, is considerably larger than the other. On the other hand, nodular thyroids may still retain considerable resemblance to symmetrically enlarged thyroids. Adenomas may undergo almost any form of degeneration—cystic (though true cysts are rare), fatty, necrotic, hemorrhagic (recent or old), calcareous, hyaline, malignant, etc. Various combinations of these may be found in the same gland following the primary condition of multiple adenomas.

Symptoms.—Non-toxic goiter can produce symptoms only by pressure incident to its size. These symptoms are dependent not only on the actual bulk and shape of the gland, but also on the

tionably a group of cases in which a more or less constant train of symptoms in varying degrees of intensity is present. These cases Plummer[5] has classified as the toxic non-hyperplastic, and he has statistically shown that clinically they are quite distinct from the exophthalmics. For instance, patients of this group give an average history of the goiter appearing at twenty-two years of age, and the first symptoms of intoxication at 36.5 years of age. The corresponding ages for patients with exophthalmic goiters are thirty-two and 32.9 years, that is, the symptoms appeared only a few months following the first evidences of goiter. He has also shown that of the non-hyperplastic goiters, 23 per cent. were toxic and 77 per cent. atoxic. Assuming that the association of the constitutional symptoms with the goiter was to some extent a personal equation, this estimation was made on a very conservative basis.

Pathology. The pathologic findings in this group of cases are not constant. Wilson[18] found that the picture of the cases resembling exophthalmic goiter is one of increased parenchyma through regenerative processes in atrophic parenchyma, or the formation of new parenchyma of the fetal type, with an increase of secretory activity and absorption. In the cases of toxic non-hyperplastic goiter with marked cardiovascular symptoms the pathology much more closely resembles the so-called simple goiter.

Symptoms. The symptoms in the group of patients who, having had a goiter for some years, gradually develop constitutional evidences of an intoxication, are not constant. As these patients come to examination the one prominent feature is the apparent selective action the toxin possesses for the cardiovascular system. Myocardial changes predominate, and in so far as actual serious injury to cardiac muscle is concerned, it is much more marked than in the true exophthalmic type. Other symptoms are relative and vary greatly in intensity, but with the nervousness and tremor usually less obvious than in the hyperplastic group. The development of practically all the symptoms in the majority of cases is gradual, progressive, and certain. The course of the toxemia rarely exhibits the rise and fall in severity of a pure exoph-

thalmic, but rather the continued poisoning does not permit of any marked tendency to a return of normal health, and leads to irreparable damage of vital organs and the establishment of secondary changes, particularly myocarditis, arteriosclerosis, etc. In advanced cases the symptoms and the goiter are sufficient to make a diagnosis, yet any connection between the thyroid and the constitutional state is frequently overlooked. In general this group, as Plummer has pointed out, corresponds very closely to the cardiovascular complex resulting from long-continued alcoholic, luetic, septic, and other toxins.

In correlating the symptoms it is, of course, essential that it be first determined, if possible, whether the goiter is responsible for the intoxication. Having decided this, it is then necessary to exclude the true exophthalmic type. In many cases there is no difficulty experienced in recognizing from the symptoms alone that the condition is totally different from that seen in the exophthalmic, but it is also true that in some patients it is impossible to say definitely from clinical evidence that the case is not one of Graves' disease. Plummer believes that the pathologic picture sharply separates these two groups, inasmuch as true exophthalmic goiter does not exist without hyperplasia of the thyroidal elements, and if the gland of this doubtful case does not show sufficient evidence of hyperplasia to be termed "hyperplastic," the case can probably be properly excluded from the exophthalmic group.

The symptomatology, therefore, exhibits two extremes. On the one hand, is the patient who consults the physician because of a goiter of some size, and with no knowledge that the gland has produced any intoxication, but in whom early cardiovascular changes can be demonstrated. On the other hand, the patient's condition may be precarious on account of the advanced degeneration in vital organs. Between these two extremes all variations occur, and these constitute a most interesting group for further study.

Treatment.—Given a toxic process of steady and certain progress and due to a definite focus, the extirpation of that focus

would seem to offer an ideal treatment for the relief of the condi-
tion. The results of surgical treatment in this group are extremely
satisfactory if the removal of the diseased portion of the thyroid
be accomplished before serious damage to the heart, kidneys, etc.,
has taken place. In the latter, operative measures entail greater
risk, but in the majority of cases operation is advisable since the
source of the intoxication is in this way removed, and thus giving
the patient an opportunity of at least partial recovery of normal
vital functions.

In the milder grades of toxemia a partial thyroidectomy is
usually permissible under general anesthesia. Careful judgment
is required in these cases as to the proper amount of gland to re-
move, the object being to extirpate as large a portion as possible
without incurring danger of a supervening hypothyroidism. In
many of these cases, therefore, a double resection is done, enu-
cleating the diseased portions of both lobes. In others, in which
the entire gross lesion is confined to a single tumor in the gland,—
a circumscribed adenoma, usually in some stage of degeneration,—
nothing more is necessary than the removal of the tumor. In the
more serious cases, with broken compensation, renal changes, etc.,
great care is necessary in the selection and conduction of the opera-
tion. In some instances it seems advisable to carry out the entire
operation under local anesthesia; in others ether throughout is
the method most suitable, while yet in others a combination of the
two anesthetics is the most satisfactory. Not only the general
condition, but the type of the patient, plays a large part in the
decision of what should be done. One may be little disturbed by
a thyroidectomy under local anesthesia, while another, apparently
in a similar physical condition, may be rebellious, and any attempt
to carry out the operation under local anesthesia may be ex-
tremely dangerous. Many of these patients have reached a state
of exhaustion, and about the limit of cardiovascular stimulation,
and any slight extra exertion may prove fatal.

This group derives little if any benefit from preparatory opera-
tive treatment. Any attempt to cut off part of the circulation
by ligation of vessels is not followed by beneficent results, and is

especially futile in the single adenomas. It is in this group that preparatory general and medical measures are particularly advisable, rest in bed with symptomatic treatment, especially digitalis, being the most essential.

The operative procedure is similar to that indicated in the non-toxic group, with the technical difficulties considerably exaggerated on account of the vascularity of the gland, its degenerative nature, and its friability.

GROUP III.—*The hyperplastic atoxic thyroids*, constituting only 0.8 per cent. of the hyperplastic thyroids coming to operation, need not be considered in this paper. The extreme rarity of a marked hyperplasia without toxic symptoms is significant in our present conception of exophthalmic goiter.

GROUP IV.—*Hyperplastic Toxic or Exophthalmic Goiter.*— There is no disease of such a definitely toxic character about which more has been written and less actually learned than exophthalmic goiter. A definition based upon our present knowledge should be that it is a disease practically always associated with hyperplasia of the parenchyma of the thyroid, and manifesting itself by a symptom-complex suggestive of a toxin which acts particularly on the nervous, cardiovascular, and digestive systems and disturbs normal metabolism.

The disease is of considerable historic interest. Parry[19] probably should be given credit for first drawing attention to the condition, while to Graves[20] and Basedow[21] belongs the honor of the most accurate early description of the disease. Undoubtedly the greatest impetus toward our recently acquired knowledge of the disease has come through the advent of the surgical treatment of exophthalmic goiter. In this connection the names of Kocher, Mayo, Halsted, and Crile will always stand out prominently.

No statements based on conclusive evidence can be made as to the etiology of the disease. There is nothing as yet to prove positively that it is due directly to an abnormal or a perverted thyroid function, but there is certainly sufficient evidence to show that the typical exophthalmic goiter is practically always associated

with hyperplastic or hypertrophic changes in the thyroid, and if these changes are not present, the disease is not exophthalmic goiter. This, however, is the only definite and constant factor known at the present time. What prompts the gland to this excessive activity, how this stimulation acts upon the gland, the nature of the toxin which is concerned in producing the constitutional symptoms, and its mode of action are all problems which have yet to be elucidated. In view of the results obtained in the removal of portions of the gland, the hypothesis seems logical that in its hyperactive state the gland secretes a substance which fails to perform its normal function of neutralizing waste-products of metabolism. The mass of evidence from the thyroid clinics of Kocher, Mayo, and Crile would prove that the intoxication at least takes place through the thyroid.

Females are much more prone to the disease than males. In the Mayo Clinic, of 2928 patients with exophthalmic goiter, 85 per cent. were females, and 15 per cent. were males. About 10 per cent. were under twenty years of age. The age of onset is usually from twenty-five to thirty-five years, the average age at which symptoms were first noted by the patient being in this series thirty-two years. The youngest individual was a girl of four, and we have seen 5 cases under ten years of age, these ages being seven, four, seven, eight, seven, and all girls.

There is no one etiologic factor which will explain any considerable percentage of cases. It is true that some patients date their first symptoms from some psychic disturbance, usually a shock to the nervous system, and that others, when partial recovery has taken place, suffer an exacerbation after a prolonged mental strain. Aside, however, from this, the etiology of the disease is in obscurity, nothing more than hypotheses up to the present time having been advanced. It is only problematic to discuss whether the hyperactivity of the thyroid is primary or is an incident in a general disorganization of the ductless gland system.

Crile[22] holds very fascinating theories as to the origin of exophthalmic goiter, believing it to be a "disease of the motor mechanism that causes physical action and expresses the emotions; its

origin is in phylogeny, and its excitation is through some stimulating emotion intensely or repeatedly given, or some lowering of the threshold of the nerve receptors, thus establishing a pathologic interaction between brain and thyroid."

Pathology.—From the mass of observations on the pathology of the thyroid in exophthalmic goiter there is one fact which stands out markedly. Wilson[23, 24] and Plummer,[16] from the study of the pathologic and clinical aspects of the question and correlating their findings, show conclusively that true and active exophthalmic goiter is practically always associated with notable hyperplasia of the thyroid. This observation is generally accepted, though with some reservations by certain men, who have probably not accurately associated their clinical and pathologic data. Many cases of chronic thyrotoxicosis which have been erroneously diagnosed exophthalmic goiter show little or no hyperplasia in the thyroid. This has led to inaccurate statements as to the supposed pathology of exophthalmic goiter.

The observations of Wilson[24] on over 1000 glands from patients with exophthalmic goiter show very definite pictures. The great majority of these glands are possessed of a hypertrophy of the parenchyma indicated by the presence of large-cell columnar epithelium with nuclei approaching the free extremities of the cells. Parenchymatous hyperplasia was also found in all this series. Hypertrophy and hyperplasia are marked by a progressive increase in the size of the acini. The shape of the acini also varies directly as to the amount of hypertrophy and hyperplasia. The cytoplasm also becomes more granular. The nuclei, whenever the epithelium approaches the columnar type, are perceptibly swollen. The amount of secretion within the acini varies with the stage of the disease—the more advanced the process, the greater the amount of secretion and the greater its density. Wilson has also shown that there is evidence that thyroid parenchyma which has been atrophic may later regenerate. He believes that the pathologist, working without the corroboration of the clinician, cannot only diagnose true exophthalmic goiter from the microscopic picture, but also estimate, with about 80 per cent. of accuracy, the stage

of the disease, and with about 75 per cent. of accuracy the severity of the disease, by correlating the weight of the gland removed, character of blood-vessels, amount of stroma, size and shape of the cells, amount of hypertrophy and hyperplasia of the parenchyma cells, and the amount and density of secretion contained within the acini.

Symptoms of Exophthalmic Goiter.—Any disease of such a protean character as exophthalmic goiter, and which exhibits such irregularities, must of necessity be the subject of widely varying statements as to the symptomatology. In the first place, the accepted name of the disease has brought about endless confusion, in that in some countries, particularly in England, undoubted cases are not designated exophthalmic goiter unless exophthalmos is present. So frequently unquestionable cases are seen in which there is no exophthalmos that coining a new name for the disease has many times been suggested. It is, however, a fact that practically all the true cases at some time develop exophthalmos, although it may be late in the course of the disease. It, therefore, appears to be more convenient to discuss individual symptoms and in the order of their frequency.

Plummer,[16] from statistical data based on 2928 cases, finds the order of onset of the most important symptoms as follows: (1) Cerebral stimulation; (2) vasomotor disturbances of skin; (3) tremor; (4) mental irritability; (5) tachycardia; (6) loss of strength (weight); (7) cardiac insufficiency; (8) exophthalmos; (9) diarrhea; (10) vomiting; (11) mental depression; (12) jaundice; (13) death.

1. *Cerebral Stimulation.*—By the patient and friends this symptom is usually referred to as nervousness. Most commonly it is evidenced by a mental restlessness which is very characteristic. These patients in every action appear to be under the influence of some stimulating intoxicant. This condition exists in all variations and follows closely the degree of toxemia. In an acute hyperthyroidism the cerebral manifestations are extreme, and, in a patient with an intoxication severe enough to produce death, the cerebral symptoms are almost typical of delirium tremens.

In the earliest evidences of the disease this cerebral stimulation is noted not only in the mental unrest, but in the motor activity set up by the abnormal stimuli, so that many of these cases exhibit mild choreiform movements which are quite characteristic.

2. *Vasomotor Disturbances.*—The most common is sweating, which may be very excessive, involving principally the palms of the hands. Flushing of the face and neck are common, and various other manifestations of vasomotor abnormalities exist, as pruritus, localized edema, etc.

3. *Tremor.*—This condition is present in the vast majority of cases. It is usually fine and rapid (8 to 10 to second), but sometimes coarse and associated with great muscular weakness.

4. *Mental Irritability.*—This state is but a variation of the cerebral stimulation, and is common. One of the most frequent complaints made by patients is their dread of the presence of other people, even of members of their own family. Unusual noises, rollicking children, and any outside influence is followed by an exacerbation of this symptom.

5. *Tachycardia.*—Inasmuch as the toxin gives every evidence of having a selective action for vital systems, along with a stimulated nervous system we find an abnormal cardiac activity as one of the earliest and most constant signs of an exophthalmic goiter. At first this may not be perceptible to the patient, and in many instances, in the absence of definite other symptoms, when discovered, is considered "palpitation." In those patients in whom the enlargement of the gland is slight and in whom no exophthalmos exists, because of the relative prominence of the tachycardia, the condition is often erroneously diagnosed as a functional cardiac disorder. The pulse-rate varies very much according to the degree of intoxication and also with the physical activity and mental status of the patient. Continued stimulation brings about, of necessity, permanent changes in the cardiovascular apparatus.

6. *Loss of Strength.*—This may practically be put down as a cardinal symptom of exophthalmic goiter. In almost all patients with Graves' disease muscular weakness is present in varying degrees, and is exceedingly marked in severe cases. The weakness

is often most striking in the hamstring group of muscles, and the patients' difficulty or inability to step onto the foot-rest of an examining table is very characteristic. In the histories of patients with exophthalmic goiter the expression "tires easily" occurs with significant regularity. Coupled, in the majority of patients, with the loss of strength is a loss of weight, which most frequently is relative to the degree of intoxication, yet in some very severe cases a rapid gain in weight occasionally takes place during a remission in the acute symptoms.

7. *Cardiac Insufficiency.*—Sooner or later in the course of a definite Graves' disease the heart exhibits evidences of a damaged muscle. This may be shown in dilatation, hypertrophy, incompetent valves, irregularities, thrills, and general evidences, such as the edema and anasarca, of an inefficient cardiac action.

8. *Exophthalmos.*—It is significant that a disease so many times should be found lacking the very symptom which gave it its name. Notwithstanding the fact, however, that in the average patient several symptoms precede exophthalmos, yet in well-advanced cases eye changes are more or less constant. The staring described by Stellwag,[25] widening of palpebral fissure (Dalrymple[26]), lagging of the lids with eye movements (Graefe[27]), and insufficiency of accommodation at near points (Möbius[28]) are seen with relative frequency.

9, 10. *Diarrhea* and *vomiting* show the effect of the toxin on the gastro-intestinal tract and indicate a severe degree of intoxication. Very seldom is either controlled by any medication, but seems dependent on the toxemia, and may, therefore, follow closely the curve of the general manifestation of the disease. Either or both of these symptoms may continue to the point of exhaustion and death.

11. *Mental depression* is one of the most definite evidences of a high grade of toxemia, and often is of serious import.

12. *Jaundice* indicates hepatic degeneration, and, if marked, is usually associated with edema and ascites. It is the symptom marking a general toxemia from which few recover. Besides these symptoms, which are given in the order of their onset, other clin-

ical manifestations upon which we may base a diagnosis of exophthalmic goiter must be here considered.

The Thyroid.—In the series of cases which have come to operation in the Mayo Clinic the thyroid has shown more or less enlargement. It is, however, also true that in some of the most severe cases, and in some patients who have died without operation, it has been difficult to palpate the thyroid, although at postmortem some increase in size has always been demonstrated. As a rule, the gland is readily palpable; it is hard, sometimes nodular, and conforms more or less to the shape of the normal thyroid,—the so-called ''butterfly gland,''—and seldom exhibits such marked enlargement as is so frequently found in simple goiter. The true exophthalmic goiter is rarely of sufficient size to cause unquestionable symptoms of pressure.

In connection with the blood-supply to the gland, one of the most important physical signs upon which a diagnosis may be based is the presence or absence of a thrill over the superior thyroid vessels. A definite thrill is usually associated with hyperplasia and exophthalmic goiter, and is rarely present in non-hyperplastic goiter. An auscultatory bruit over the gland is common.

Blood.—Kocher[29] believes the blood-picture to be pathognomonic. He states that the number of the different varieties of normal leukocytes undergoes alteration, and that the number of leukocytes as a whole is slightly diminished. The neutrophile leukocytes are diminished to half their normal number, so that they may be less numerous than the lymphocytes; the latter are increased sometimes to twice their normal number; and even if there is no absolute increase, there is always a relative augmentation. In our clinic careful blood records have been made both before and after operation in 1500 cases of exophthalmic goiter. Our results do not substantiate Kocher's statements to as great a degree as we had hoped, and we have not been able to observe any constant relationship between the severity of the disease and the blood-picture. Menstrual disturbances are the rule rather than the exception, there being either a marked diminution in quantity or frequency or cessation of the flow.

Diagnosis.— The diagnosis may be made without difficulty in the great majority of cases which come to a surgical clinic. The questionable cases are those seen early in the course of the disease, and when major symptoms are lacking. It is at times a delicate point to settle whether in a young woman with a slightly enlarged thyroid, some mild nervous phenomena, and a quickened pulse, the picture is one of an early hyperthyroidism, a purely psychic manifestation, or neurasthenia. In most instances, however, careful observation will differentiate the conditions.

It is to be hoped and expected that there will be obtained from the blood of patients with exophthalmic goiter some substance or substances of diagnostic aid in our knowledge of the disease, and that this will afford a means of detecting these early cases. Following out the original investigations of Schönborn[30] and Gley[31] on the effect of extracts of simple and exophthalmic goiter, Blackford and Sanford[32] have demonstrated, in a series of 46 exophthalmic and a similar number of simple goiters, the following facts:

"Fresh extracts from the glands of patients with exophthalmic goiter contain a powerful depressor substance. A similar depressor substance exists in the serums of these cases, and this is present in direct proportion to the clinical acuteness and severity of the disease. The serums of patients with non-hyperplastic thyroids do not have a depressor action. After the active depressor dose of serum from a case of exophthalmic goiter the depressor action of the extract of an exophthalmic goiter is weakened or abolished. The converse is also true." To the elaboration of these important findings we must look for the separation of a specific toxin, if one exists, in cases of exophthalmic goiter.

The work of Kendall[33] on the chemical constituents of sheep's thyroid apparently shows that the complex proteins of the gland may be broken down into simpler substances which still retain their original physiologic activity. These substances may be divided by chemical reactions into several fractions, and it then appears that each of these subdivisions exhibits its own specific physiologic activity. From one of these divisions a compound containing 32 per cent. of iodin has been separated; also lauric

acid and indol, in combination other than tryptophan, have been shown to be present.   The well-known physiologic action of indol suggests that this substance may be one of the toxic compounds which produces some of the symptoms of exophthalmic goiter.

Prognosis.—In estimating the prognosis in a given case several factors must be borne in mind.   These deductions will be made first on the group of cases in which we may assume that the intoxication can be arrested.   In this group we have first to consider cases of early hyperthyroidism.   It is in these patients that the most satisfactory results are obtained by preventing the further action of the toxin before it has had sufficient time to cause any permanent injury.   The second group contains those patients in whom the disease has been of sufficiently long standing or severity to cause enough physical and mental disability to prevent their carrying out their usual occupation, but who, when the intoxication is once intercepted, may recover sufficiently to return to a more or less normal habit of life, so far as pleasure and work are concerned.   Many patients with marked exophthalmic goiter syndrome, after partial thyroidectomy, have gone through pregnancy without difficulty or recurrence of symptoms.   A third group consists of individuals who may be termed "old or cured exophthalmics."   They represent a class in whom the diagnosis is certain, and yet in whom, for some years, there have been no manifestations of any marked activity of the gland.   These cases do not require treatment other than general measures.   The storm is over, the fires have burned themselves out, and there remains only the aftermath of a severe and prolonged illness.

Besides the above, there is a group of patients, fortunately small, in whom the hyperthyroidism is not amenable to treatment of any kind yet known.   These acute cases run a short course, terminate fatally, and are not associated with remissions during which any means of controlling the disease may be instituted.

Treatment.—The treatment of exophthalmic goiter may be conveniently divided into non-surgical and surgical.   It is extremely significant that, with the advent of surgical treatment of exophthalmic goiter, and especially during the last few years with

the results which have been obtained, very little has appeared in the literature relative to medical treatment. The success attending medicinal measures in all probability depends on the fact that a percentage of patients with exophthalmic goiter recover from their acute symptoms and remain in a degree of health commensurate with the ordinary duties of life. This has afforded the means of exploiting numberless remedies in the treatment of the disease.

The medicinal treatment can be summed up as follows: Rest, which is, above all, the most important, and the treatment of special symptoms. No one measure has given sufficiently consistent results to be retained as a permanent remedy. Among the many forms of treatment which have had some success may be mentioned bromids and phosphorus preparations, serum from thyroidectomized animals, the cytotoxic serum of Beebe and Rogers,[34] x-ray exposures, injection of iodin and iodoform into the gland, desiccated thymus, belladonna and quinin, thyroidectin, osteopathy, suggestive therapeutics, Christian Science, etc.

It is regrettable that statistics sufficiently large upon which to base comparisons have not been forthcoming from cases treated by non-surgical measures. The fact that, until recently, the large majority of these patients were not seen by the surgeon until medical treatment had failed made it difficult to compile definite data concerning them. Alvarez[35] says that the physician, in the absence of the surgeon, can do little more for the patient with exophthalmic goiter than he could in the time of Parry, Graves, and Basedow.

Surgical Treatment.—Careful judgment as to whether or not to operate, when to operate, just what to do, and how much to do, the proper preoperative and post-operative care, and the mastery of a difficult technic, are some of the major problems to be considered in the surgical treatment of exophthalmic goiter.

It is true that the low mortality following operations for exophthalmic goiter is due not so much to improved methods of operating, nor to a greater acquired skill, as to better judgment of the proper time to operate. Not infrequently patients are brought to the surgeon in an almost moribund condition, and to opera-

tions undertaken on these patients much of the high mortality of the earlier results can be attributed.   As C. H. Mayo[36] has pointed out, an emergency operation is never called for in exophthalmic goiter.   Patients in acute exacerbations should be put at absolute physical and mental rest until the exacerbation has subsided, when surgical treatment may be carried out in the quiescent period.

The selection of a proper time in which to operate during the course of the disease or, more particularly, the avoidance of the period of increased intoxication, is of extreme importance.   Plummer,[16] basing his observations on the histories of a long series of cases of exophthalmic goiter, has shown that, "If the average course of the intoxication be represented by a curve, the greatest height is reached during the latter half of the first year, and then suddenly drops to the twelfth month.   In many instances it reaches the normal base-line during the next six months.   More often it fluctuates with periods of exacerbation for the next two to four years.   Secondary symptoms and exophthalmos may remain, but the active course only rarely continues over four years without distinct intermissions.   Compare the striking resemblance of the character, order of onset, and course of this train of symptoms with that resulting from the heavy use of alcohol by a susceptible individual over a corresponding period of time.   Near the crest of the curve any shock, operation, etc., that treats the patient to another drink may result in tremens or death."   This observation explains the occurrence of an acute hyperthyroidism after a mental shock, accident, or a ligation under local anesthesia or a thyroidectomy.   At this period the disease is not surgical, and should be treated by medical measures until the acute exacerbations have ceased.

"In the average course, after the first year, the symptoms that may be attributed to long-continued intoxication rather than to a high degree of acute intoxication, i. e., those from the more chronic types of heart, liver, and degeneration of the kidney, enter strikingly into the clinical picture.   In attempting to construct a composite curve we find that the curves for those symptoms that

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we can readily attribute to a high degree of immediate intoxication from the thyroid gradually drop, while the curves for those findings attributable to a long-continued intoxication of a lower degree, gradually rise."

What should be the operative procedure? In the majority of instances it is possible to decide definitely at the time the patient is seen as to what should be done. In many the condition is such that a primary partial thyroidectomy may be made with safety; in many, as a precautionary measure, a preliminary ligation of one (usually the left) superior pole is advisable; while in yet others a double ligation is the proper course. Many factors are to be considered in deciding as to what the patient may have done with reasonable safety. The degree of intoxication, the length of the history, the weight-balance during the preceding two or three months, the muscular weakness, the cardiac symptoms, especially the amount of dilatation and the mental stability, must all be taken into account. Plummer believes that the mental state may be counted upon as the most valuable single indication of what the patient is able to undergo.

The value of a preliminary ligation, in the questionable and in the more severe cases, is undoubted. This method of treatment has probably had more to do with successful results than any other one factor.

The proper operative procedure in many cases is immediately apparent; in others it is not possible to decide the character of the operation until the patient is on the operating table, although with increasing judgment this is less frequently true. In uncertain cases the fixed rule is to give the patient the benefit of the doubt and keep on the safe side. Frequently on the morning of operation an exacerbation of symptoms over the preceding day is seen, and various methods have been employed to prevent this. Among these Crile's[37] may be mentioned as the most interesting. He endeavors to perform the operation without the knowledge of the patient, but surreptitious operations are apparently not necessary. Besides the disadvantage of not having the helpful co-operation

of the patient, there exists in the patient's mind an uncertainty which does not foster a quiet and desirable mental state.

In the average case, granting that a ligation is advisable, the operation is accomplished in the following manner: After anesthesia by an infiltration of 0.05 per cent. novocain, an incision about two inches in length is carried outward from the middle of the thyroid cartilage, choosing, if possible, a natural crease in the skin. The platysma muscle is reflected with the skin and subcutaneous tissues. The anterior border of the sternomastoid is isolated and tracted outward and the omohyoid inward. The exposure thus gained brings to view the pole of the gland with its vessels. The entire blood-supply of the pole is then encircled by an aneurysm needle threaded with silk, and the vessels, or the pole if it has been transfixed, tied.

Postoperatively, quiet, salines by bowel,—or, if not retained, subcutaneously,—ice to the precordium, occasionally morphin, and still less frequently digitalin, are the measures most used in the care of these patients. The further management of the case depends on the constitutional reaction following the ligation. If the patient's condition is not exacerbated to any great extent, and if the pulse-rate lowers within forty-eight hours to a point below 100 and remains there, the patient may safely go through with an extirpation of a large part of the thyroid in a few days. If, however, a marked exacerbation of symptoms occurs and the patient's condition becomes at all serious as a result of the ligation, a ligation of the opposite pole should be done, and thus the patient be given an opportunity of obtaining the benefit incident to a diminished blood-supply to the gland. This improvement is reasonably certain and is evidenced in almost every way. The patients not only gain in weight (the average in a large series is about 22 pounds), but in strength, mental condition, and give every evidence of a lessened toxemia. The height of the improvement is usually about three months after the double ligation, and the partial thyroidectomy may then be performed with practically no risk.

The partial thyroidectomy in exophthalmic goiter requires careful and experienced technic. Ether administered by the open

method by a skilled anesthetist is preferable to local anesthesia, gas, oxygen, or any other anesthetic yet devised. The shock to these patients is more dangerous when they are cognizant of what is going on.

The technical difficulties are dependent on the fact that the markedly hyperplastic thyroid is highly vascular, friable, with firmly adherent capsule and brittle vessels. All these conditions are particularly marked in thyroids removed following ligation. It is unnecessary to go into the details of the classic operation of Kocher, which has been elaborated in this country by Mayo, Crile, and others. Suffice to say that good exposure is essential with careful clamping and ligation of all vessels and the secure suturing of the retained stump of gland. The intracapsular (posteriorly) dissection advocated by Mayo[38] in order to avoid injury to the nerve or parathyroids is important.

The question of how much of the thyroid should be removed is of necessity important and is still open to discussion. In our clinic the removal of a large part of the hyperactive gland is practised, and, so far as is known, there have been no symptoms which might be due to deficient thyroid secretion in any of the patients with exophthalmic goiter. The entire right lobe, isthmus, and a part of the left lobe, sometimes as much as four-fifths of the active gland, should be removed, as a rule. It is not at all unlikely that, in performing a so-called total extirpation of a lobe, small, almost imperceptible pieces of gland tissue may be retained which will perform a part of the thyroid function. Although the tendency is to remove more of the gland, yet practically never is less gland retained than the size of the normal gland. Drainage in these cases is established by a rubber tube left in for twenty-four hours. A considerable percentage of cases may safely be closed without drainage. The further treatment of the partially thyroidectomized patient is symptomatic with advice against mental or physical strain until full benefits are derived. Should a recurrence of symptoms take place, due to overactivity of the remaining portion of the gland, a resection of a portion of the remnant may be made.

As to the results of the surgical treatment of exophthalmic goiter, even conservative reports are extremely gratifying. Kocher[39] has recently reported a series of cases in which 83 per cent. were cured. In this country statistics are perhaps a little more conservative, varying from 70 to 75 per cent. cured and a very small percentage not cured. Statements of the results of the treatment of exophthalmic goiter are questionable in accuracy and have insufficient bases for comparison. As before mentioned, no large group of cases have ever been published reporting the non-surgical course of the disease, hence surgical reports must rest on their own foundation, inasmuch as the uninterrupted course of the disease is not accurately known. One cannot logically say an exophthalmic goiter is cured as long as any of the original symptoms persist to even a slight degree. The verdict of the patient, however, seems to be a fair standard of results. About 75 per cent. of those operated on report themselves as cured—that is, enjoying a useful and profitable life. This is an extremely good percentage when one considers that the treatment in many cases was not only of the acute disease, but also of the more chronic conditions, when permanent changes have become established. Even in these, cutting off the supply of toxin has allowed the damaged organs to at least regain a part of their normal function. In considering statistical data one cannot be certain of the period the symptomatic cure will last. Years later relapse may take place.

The operative mortality constitutes the least of the surgeon's worries at the present time. Proper selection of operative time and procedure will keep the mortality in the neighborhood of 1 per cent. Large series of operations may be accomplished without a death. In our clinic a year ago 275 consecutive operations on exophthalmic goiter were made without a fatality. Thyroidectomy following double ligation is practically always safe. Mortality is almost entirely due to "acute hyperthyroidism" or acute dilatation of heart. The accidents and complications incident to other operations, such as pneumonia, embolism, hemorrhage, etc., rarely occur in surgery of the thyroid.

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HEAD, TRUNK, AND EXTREMITIES

TUMOR OF THE MIDDLE CRANIAL FOSSA INVOLVING THE GASSERIAN GANGLION*

WILLIAM A. PLUMMER AND GORDON B. NEW

Cases of tumor of the middle cranial fossa involving the gasserian ganglion are rarely seen and but rarely reported in literature.

In 1908 Spiller† reported two cases which had recently come under his observation. He also reviewed one case presented by Keen, Dercum, and Spiller, and one reported by Hofmeister and Meyer in their paper on "Tumor of the Gasserian Ganglion." A few other cases have been noted in literature.

The case here reported was a tumor of the middle cranial fossa involving the gasserian ganglion:

History.—O. R. (Case A77175), a well-developed man, aged twenty-one, was examined December 10, 1912. Family history was negative for tuberculosis or other chronic diseases, and personal history good, without evidence of syphilitic infection or alcoholic excesses. Three enlarged upper cervical glands had been discovered on the right side of neck twenty-one months previous to examination. Three months later pain developed anterior to the right ear, and the local physician excised the glands, which were thought to be tuberculous, although no microscopic examination was made. From that time until the patient came for consultation pain had been constant in the site of the trouble, with intermittent, tic-like paroxysms over the entire distribution of the right fifth nerve. The paroxysms occurred once or twice a day and lasted from a few minutes to an hour. Momentary attacks of diplopia and of indefinite objective vertigo were complained of. Following the operation on the glands there had been some stiffness in using

the lower jaw.   Six weeks previous to our examination deep alco-holic injections of the branches of the fifth nerve had been made with some relief for one week.   Two weeks following this procedure an operation was done in the right temporal region, but there were no data to show what was accomplished.   For one week prior to coming to our clinic there had been a drooping of the right upper lid.

Examination.—General examination disclosed nothing of note. All reflexes were normal; there was no ataxia in station or gait. Mentally the patient was rather dull and apathetic, and answered questions slowly.   A superficial survey of the head revealed a scar on the cheek following the use of a hot-water bottle, as well as those left by the previous operations.   A small trophic ulcer was appar-ent on the right side of the upper lip, below and to the right of the nasal ala.   The sense of smell seemed to be slightly diminished on the right side.   There was a marked ptosis of the right upper lid. The right pupil was dilated and showed no reaction to light or accommodation.   There was partial paralysis of all the extrinsic muscles of the right eye, but this was less evident in the external rectus.   Vision in the right eye was 20/50, with slight contraction of the fields.   The optic nerve-head was pale.   Vision in the left eye was 20/20; the fundus, extrinsic muscles, reflexes, and fields were normal.

Careful tests showed anesthesia and analgesia of the skin and mucous membrane supplied by the first and second divisions of the right fifth nerve, with hypesthesia and hypalgesia in the distribu-tion of the third division.   There was also complete anesthesia of the right cornea.   A slight exaggeration of the jaw-reflex was noted; the pharyngeal reflex was apparently normal.   The sense of taste was absent in the right anterior portion of the tongue.   The tongue could not be protruded beyond the lips, as it was impossible to separate the teeth more than 1/2 inch, which condition was prob-ably the result of contracted scars following the previous operations. No weakness of the tongue muscles was evident.   There was a definite decrease of strength in the muscles used in closing the right side of the jaw.   A specimen from a slight bulging of the right side of the nasopharynx showed lymphatic tissue only.   There was a slight bilateral catarrhal deafness.   The sinuses were objectively normal.   A roentgenogram of the skull disclosed a trephine opening about 1/2 inch in diameter in the right temporal region.   Diagnosis was made of a tumor of the middle cranial fossa involving the gasserian ganglion.

Operation.—June 6, 1913, an operation was performed in the Mayo Clinic by Dr. Beckman. The Hartley-Krause method exposed a hard mass below the right temporal lobe. The extent of the tumor could not be determined, and it was considered inoperable. A specimen examined microscopically showed the tumor to be a small round-cell sarcoma.

The patient died a few months later. No necropsy data were obtained.

The important features in this case are: (1) The enlargement of the right cervical glands; (2) the constant dull pain just anterior to the right ear, with paroxysms of sharp pain which involve the entire distribution of the fifth nerve; (3) the absence of symptoms of general intracranial pressure, such as headache, vomiting, choked disk, etc., unless the occasional vertigo and the mental hebetude are considered symptoms; (4) the definite localizing signs, such as the anesthesia, the loss of the sense of taste on the right anterior portion of the tongue, the partial paralysis of all the right extrinsic eye muscles, with a nearly complete ptosis, the pallor of the right optic nerve-head, and the large, immobile right pupil.

It is possible that the anesthesia became more definite following the alcoholic injections which had been given six weeks previous to our examination. As would be expected, considering the absence of any signs of general intracranial pressure, there was no improvement following the exploration.

In the cases reported by Dercum, Keen and Spiller, Hofmeister and Meyer, and Spiller there was enlargement of the lymphatic glands of the neck. In our case, although no microscopic examination was made by the physician who excised the glands, the history of glandular enlargement just previous to the onset of the symptoms gives strong presumptive evidence of their metastatic character.

The fact that the glands were enlarged three months before the onset of pain makes it probable that the tumor originated from the dura and had gained considerable size before it involved the gasserian ganglion.

EPITHELIOMA OF THE LIDS*

CARL FISHER

Epitheliomas of the lids require some consideration apart from epitheliomas of the skin elsewhere, because of their proximity to the orbit and sinuses and because of the disastrous effects of destruction of the lids on vision and on the appearance of the patient. A good proportion of these patients do not consult the ophthalmologist, but are sent to the general surgeon after a long course of salves, pastes, and Roentgen-ray treatment.

I have been able to study 88 cases of epithelioma primary in the lids and canthi, or involving them from the skin in the immediate vicinity (nose, cheek, brow), having chiefly in mind the prognosis of operative treatment. The statistical data were collected to serve as a basis of comparison with other methods of treatment, especially radium. It should be added that the diagnosis in all cases was confirmed by microscopic examination.

The epitheliomas of the lid all belonged to the type known as basal-cell, or, to use a rather popular term, rodent ulcer. By this is commonly meant clinically a cancer of the skin of very slow growth, with no tendency to glandular metastases, spreading by continuity, and usually ulcerating as it progresses. Pathologically, it is somewhat more difficult to define, though this is perhaps of no great consequence to our present object. Adami[1] sums up the present view of this class of epithelioma:

Krompecher, recognizing that all conditions classified as rodent ulcer do not belong to the type, has labeled this form basal-cell

carcinoma, on the mistaken ground that, as it shows no prickle-cells nor keratinization, it is derived wholly from the basal, undifferentiated cells of the rete Malpighii. But this is so also for all epitheliomas. In the more highly developed forms the prickle-cells present do not arise from preëxisting prickle-cells, but also from basal mother cells. It is the stage of undifferentiation and anaplasia—the capacity to develop beyond a certain point—that determines the form of the cells.

After the growth has progressed, both basal and squamous cells are to be found in the field, one or the other predominating. Some-

Fig. 159.—Epithelial down-growth, showing spindle and oval cells, which, when in masses, often look like sarcoma cells.

times the appearance may closely simulate sarcoma from the tendency of the epithelial cells to assume spindle forms. I have seen this mistaken diagnosis made several times in epitheliomas of the orbit (Figs. 159 and 160).

In this series the average age of incidence was fifty-three years. The youngest patient was twenty-four years old. The average patient waited five years before coming for treatment; many of them, from fifteen to twenty-five years; these latter mostly began as keratoses and small, wart-like nodules. Some developed rapidly, that is, in one month.

The favorite points of origin were the lower lid (46 per cent.),

the inner canthus, over the lacrimal sac (36 per cent.). The next most common point of origin was the upper lid and, least common, the outer canthus.

Of the cancers of the lid, considerably over half originated in the skin of the lid just away from the cilia, the others starting indifferently on the very margin of the lid or the base. There seems to be no obvious reason why the lids should be so favorable a site for the development of epithelioma. The fact that the lower lid and inner canthus are so much more commonly affected might be attributed
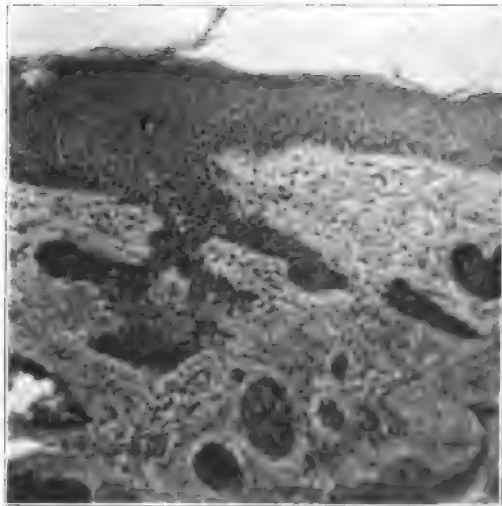
Fig. 160.—The same as Fig. 159, except growth is taken from nose.

to the irritation caused by tears and foreign matter. Certainly these regions are usually hyperemic when the upper lid and outer canthus show comparatively little evidence of irritation. In only one case was the pressure from eye-glasses a probable source of the initial irritation, which is so commonly looked for. The type of skin well recognized as a fertile soil for epithelioma—a dry, rubicund skin, seen most often in blond people exposed to the elements —was very often seen, but by no means predominated.

The majority of these cancers progressed by invasion only, the

first step being attachment to the periosteum of the orbital border, then progression into the orbit and conjunctiva. In several cases the inner orbital walls were destroyed. Occasionally the antrum was involved, and more often the ethmoids, rendering successful operation very difficult.

In five cases cervical or parotid glandular involvement was present when the patient was first seen. These two groups of glands drain all the skin and the conjunctiva, while the orbit drains into the internal maxillary group and thence into the deep cervical. Unsuccessful treatment seems to favor glandular involvement, since of these five patients only one had escaped pastes or Roentgen rays previous to examination in our clinic, and about the same proportion was found in epitheliomas of the cheek with glandular involvement. The type of tumor did not differ microscopically in these cases from that in cases not showing glandular involvement, so that the failure to involve glands is not a necessary characteristic of rodent ulcer. Our pathologic records, however, do not indicate the character of the metastatic growth. None of the patients developed enlarged glands after coming under our observation, which may have been due to the methods of treatment employed.

These patients were treated chiefly in three ways—radical excision, excision with actual cautery of the wound, or simply actual cautery, the method employed depending on the site of the growth and the degree to which it had progressed. Purely cutaneous growths, if small, were cauterized. Growths involving the border of the lid, but not adherent to the periosteum, were excised, and a plastic operation done to restore the lid. Where the growth was adherent to periosteum or had involved conjunctiva and orbit, or tear-sac, actual cautery was added to excision. In cases of orbital involvement not readily accessible an exenteration of the orbit, including the periosteum, was performed and the contents of the apex cauterized. For cauterizing large areas, the soldering iron was found preferable on account of the deep cooking given the tissues—a principle used in Percy's treatment of cancer. Involved sinuses were opened, cureted, and cauterized in so far as possible.

'14—26

The plastic repair of the lower lid is a frequent problem. Many satisfactory results were obtained from the transplantation of a "hammock" flap of skin from the upper lid, a method devised by C. H. Mayo. This flap is soft, of the same color as the normal lid, and grows readily. The operation recently described by Gibbon[2] promises to be the one of choice when the lower lid has been largely destroyed. No conventional method will serve every case. The repair is easy when a fair amount of the lid has been left. When, however, the entire lid and part of the cheek have been removed, as is often necessary, large flaps from the temple (as noted in the textbooks) give the best results. The Dieffenbach and similar procedures, beautiful on paper, have not proved so successful on patients.

RECURRENCES

This has no reference to final cures, but refers to any recurrence whatever taking place after operation in our clinic. Most of these were small nodules, easily burned off. Of the 33 epitheliomas involving the lids and canthi alone (adherent or not adherent), 17 per cent. recurred at some time. These recurrences were all at the site of the previous growth, and not in glands. When, however, the growth had penetrated the orbit, the percentage of recurrence rose rapidly—8 out of 11. Of 13 cases involving the orbit, primarily and secondarily, three have passed the one-year period without recurrence. Four others have not yet recurred, but have not gone a year since operation. The time-limit of one year is somewhat arbitrary, but is based on the average time before recurrence, namely, nine months. This is a rather high average, being brought up by a few unusual cases which were reported as having recurred very late.. The majority of cases which recurred at all did so in three to four months.

The chief interest in these cases for the clinician lies in the ultimate prognosis. I have not counted as cures cases of less than one year's standing since the last operation or treatment. Naturally, the percentage would be considerably higher if cases of over four months' standing were cited and if all patients were willing to return at the first sign of recurrence.

Of the 33 epitheliomas of the lids and canthi, not including the orbit, in which the records have been completed by recent news of the patients, 94 per cent. were cured by operation. When the orbit was involved, the percentage was turned about; 80 per cent. were not permanently cured. These include cases in which the sinuses also were involved. The factors which mitigate against cure are: inner canthus involvement, penetration of conjunctiva or lacrimal sac, orbital involvement, and sinus involvement. The cases of glandular involvement cannot be classified because our records are not completed, owing to the lack of recent information of these patients. The one "completed" case had no recurrence after a radical local removal and dissection of the cervical glands.

The comparison of these results with those obtained by the use of radium or Roentgen rays or pastes is difficult because of the absence in most papers on the subject of definite data regarding the duration of the cure. Williams and Ellsworth,[3] however, are not remiss in this regard. Of the 19 cancers of the skin of the lids, two-year cures are reported in 13 cases, or 68 per cent. These are evidently not intended to include cases with orbital involvement, since one case of orbital involvement is listed separately. The percentage of two-year cures by operation in our series was 84.

Pinch,[4] in a report of the Radium Institute of London, classified his cases of rodent ulcer into apparently cured, 31; "improved," 41; not improved, 12; abandoned treatment, 6. Counting improved, not improved, and abandoned as failures (as was done in our series), the percentage of cure is far from satisfactory (about 39 per cent.), and this without any minimum time-limit set. It should be said, however, that these were rodent ulcers of various regions and severities, so that the comparison is not altogether fair. Pinch was able to state on this showing that "rodent ulcer is of all cancers the most amenable to radium treatment." Turner[5] cured 6 out of 9 completed cases of rodent ulcer of various parts of face and lips, or 66 per cent., time not stated. The best opinion at present concerning radium versus operative treatment of these cases is well summed up by Knox.[6]

"1. In all cases of early cancer, the operative method is undoubtedly best; it is quicker, safer, and offers the best prospect of cure. . . . 3. In patients who refuse operation or are otherwise unfit for operation, radium is a useful remedy."

Comparison of operative treatment with pastes is also difficult. I have found no recent records sufficiently exact to afford a statistical comparison. Perhaps the most revolting, because easily avoidable, pictures of malpractice that one sees are cases of cancer of the skin treated with various pastes, and the inevitable impression received is that the public has suffered unspeakably from the exploitation of the paste treatment. Nevertheless, it must be acknowledged that in the hands of persons practiced in this procedure many surprising cures are obtained, and these sometimes in apparently inoperable cases. No doubt the continued financial success of certain "cancer institutes" is maintained by a fair number at least of noteworthy cures.

The Roentgen ray is believed to owe what efficiency it possesses to a ray corresponding to the gamma ray of radium, so that there seems to be no reason for preferring it to the latter (save its greater accessibility), since the curative rays are acknowledged to comprise only a small part of the whole Roentgen ray. In point of fact, the Roentgen ray cannot be regarded as a dependable agent in the treatment of epitheliomas, however useful it may be as a palliative or postoperative measure.

The present evidence seems conclusive that operative measures are, in general, the safest means of treatment we possess for epitheliomas of the lids (and for that matter in any other region), and especially when the growth is rapid and adherent to periosteum or involvement of the orbit has taken place or evidently will soon take place. On the other hand, when the patient can be kept under observation until a cure is completed and the growth is proceeding slowly, there seems to be no good reason why radium should not be used. In cases of this kind, however, it has the disadvantage of slowness, and there is also the difficulty, in most places, of obtaining the radium. But many patients prefer any amount of treatment to the use of the knife, a psychologic factor that is heavily featured

in the advertisements of the clever charlatans. The cosmetic results of successful radium therapy are excellent; I have seen no injury or reports of injury to the eye from its use; it is practically painless. In this as in any therapeutic or surgical measure, the experience and ability of the physician in charge play an important rôle, especially in pioneer work with comparatively new methods of treatment.

The importance of early and radical operation in epitheliomas with. orbital extension is well emphasized in the statistical data given above. Unless the growth is so clearly circumscribed that complete removal without sacrificing the eye is certain, a complete exenteration of the orbit followed by cautery is imperative. Extension to the sinuses renders the prognosis nearly hopeless; in such cases, if operation is decided on, it should be followed by the persistent use of radium or by Roentgen ray if the former is not available. Glandular involvement, without orbital extension, does not necessarily indicate a bad prognosis, granting that a proper resection of the gland-bearing fascia be made.

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THE SURGICAL TREATMENT OF FACIAL PARALYSIS*

EMIL H. BECKMAN

The first attempt to cure complete facial paralysis by surgery was made in 1895 by Ballance and Stewart,[1] when they united the distal portion of the facial nerve to the side of the spinal accessory nerve. In 1898 Faure[2] united the trunk of the facial to the trapezius branch of the spinal accessory, the branch being divided, with end-to-end anastomosis. In 1899 Kennedy[3] divided the facial nerve for facial spasm and united it to the spinal accessory end to side. The rationale of this work is based to a large extent on the conclusions published by Ballance and Stewart in 1901, as well as on those of other members of the so-called "peripheral school." According to these observers, regeneration occurs in the distal segment of a divided nerve, even when it is separated from its central connection. Such regeneration does not reach maturity unless the distal is again joined to the proximal segment, permitting transmission of impulses between the nerve-centers and the periphery. This regeneration, however, is sufficient to maintain the isolated peripheral nerve in a fairly healthy state even for years. It also preserves the end-organs; thus, when the peripheral nerve is finally anastomosed with a healthy proximal nerve segment, under favorable circumstances almost complete regeneration takes place, causing normal muscular contractions in the area supplied by the distal nerve. It, therefore, seems advisable in most cases of facial paralysis, especially in those where the injury to the nerve has been proximal to the stylomastoid foramen, to attempt anastomosis of the

distal segment to a healthy motor nerve-trunk for the cure of this distressing and disfiguring paralysis.

Manasse,[4] in 1900, and Barrago-Ciarella,[5] in 1901, showed by experimental work on animals that anastomosis between the facial and spinal accessory uniformly leads to complete restoration of movements in the facial muscles in about six months, the first evidences of regeneration occurring at about four and one-half months.

Since the work of Ballance and Stewart, a number of cases have been reported in the literature. Two nerves in particular have been selected as suitable for anastomosis with the divided end of the facial: the spinal accessory and the hypoglossal. The reasons given for favoring the use of the hypoglossal are: that its nerve-trunk is larger; the proximity of the cortical centers of the facial and hypoglossal nerves; some of the fibers of the two nerves have a common origin, and their centers are closely connected by association fibers, thus making cortical education and control easier after operation; the associated movements, when present, are not visible. Against the use of the hypoglossal is the argument that the difficulties of deglutition, phonation, and mastication, and the paralysis of taste on the anterior half of the tongue, are much more distressing to the patient than the disability resulting from cutting the spinal accessory. In a recent case reported by Welty[6] the atrophy of the tongue after three years was so extreme that speech was interfered with to a marked degree. He states that this would have been a serious handicap to any one required to use the voice in earning a livelihood. It would seem that the spinal accessory is preferable because of its accessibility, its motility allowing union without tension, and the relatively small importance of the paralysis and shoulder droop resulting from cutting the nerve. Soon after regeneration occurs the visibility of associated movements between the shoulder and facial expression is particularly annoying, but continued education of the cortical center in time almost entirely overcomes this difficulty.

There can be no doubt that facial paralysis is more distressing to a patient physically and mentally than the paralysis resulting from the above methods of attempted cure. The operation is

applicable to all cases of paralysis of the main trunk of the facial nerve. It has been used successfully in paralysis resulting from mastoid operations, suppurative otitis media of long standing, fractures of the skull involving the petrous portion of the temporal bone, traumatic and operative injury after exit from the stylomastoid foramen, and Bell's palsy showing complete reaction of degeneration after several months' treatment. The length of time the paralysis has existed seems to have no effect on the time required for recovery. One cure has been recorded after twenty-nine years of paralysis.

If the muscles respond to galvanism, the prognosis is more favorable, though absence of galvanic and faradic response is no contraindication to operation (Murphy[7]). The best results are obtained in traumatic cases, neuritis and suppurative diseases being less hopeful. The condition and degree of atrophy of the facial muscles have a marked bearing on the results, it being quite evident that if the muscle-fibers are entirely atrophied, their function resulting from regeneration is less likely to occur, even though the nerve regenerates completely (Taylor and Clark[8]).

Operation.—It is needless to say that precision of technic and gentleness of handling the exposed nerves are essential to successful results. The presence of the slightest degree of infection or the formation of scar tissue at the site of anastomosis endangers the outcome. In endeavoring to overcome these complications, and to assure a definite uninterrupted path for axon growth, several plans have been suggested:

1. Wrapping the site of anastomosis with Cargile membrane.
2. Surrounding the anastomosis with fascia or muscle (Murphy).
3. Fresh arteries hardened in formalin (Foramitti).
4. Gelatin tubes hardened in formalin (Lotheisen).
5. Absorbable magnesium tubes (Payr).
6. Surrounding the anastomosis with fresh section of vein.

The last procedure has been used in the Mayo Clinic in three cases, and I have not seen it described in the literature. The section of vein protects the anastomosis with a thin cylinder, which is already lined with endothelium and would seem to protect the

sutured ends from the encroachment of connective tissue.   In the three cases in which it was used the restoration of function has been more nearly perfect than in the one case in which the anastomosis was surrounded by fascia and muscle.   I am not able to state definitely whether this is due to the technic or simply a coincidence. We expect later to publish the results of experimental work along this line.   It is always easy to obtain a section of the facial, external or anterior jugular veins near the field of operation.   An inch or an inch and a half section of such a vein is slipped over the spinal accessory nerve before the anastomosis is made, and afterward moved along until it completely covers the anastomosis.   In all our operations, four in number, we have used the main trunk of the spinal accessory nerve and made an end-to-end anastomosis (Fig. 161).   One case has been operated on too recently to obtain results.

Case I.—(A9150.) E. T. M.   Male, aged thirty-five.   Examined in the Mayo Clinic April 4, 1912.   Three months previous he had received a stab wound with a jack-knife over the left stylomastoid foramen, resulting in immediate and complete left facial paralysis.
 Operation.—On April 8, 1912, the distal end of the facial nerve was exposed in the parotid gland and found to be divided just proximal to its main divisions.   The proximal end could not be found, and was thought to have retracted into the stylomastoid foramen.   After freshening the end of the facial it was united to the main trunk of the spinal accessory by three small silk sutures passed through the sheaths of the nerves after the manner of the stay sutures in blood-vessel anastomosis.
 It has been difficult to obtain satisfactory information regarding this patient, but on April 22, 1914, in a reply to definite questions, he stated that the left side of his face was much fuller than at the time of operation: that he could more nearly close his left eye than before the operation, but that it remained partly open at the inner angle.   He also stated that he could partially draw up the left corner of his mouth.   Efforts to raise his left arm caused the left corner of the mouth to draw up and the eyelid to quiver, showing that associated movements were present and that partial regen-. eration of the facial nerve must have occurred.   He could chew his food and remove it from his left cheek without any effort, while before the operation he was obliged to remove it with his finger. His arm was somewhat lame, but did not prevent him from per-
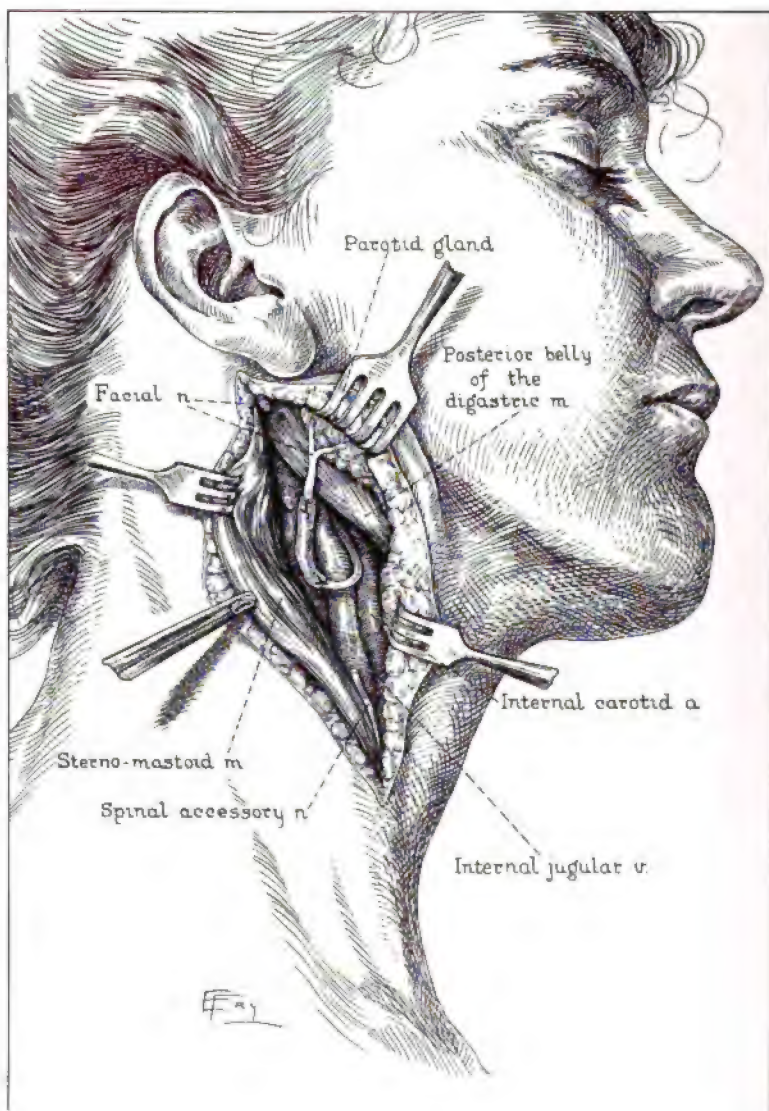
Fig. 161.—Anastomosis between proximal end of spinal accessory and distal end of facial nerve, covered with a cuff of vein taken from external or anterior jugular vein.

forming his usual labors of a farmer. He believed that he was still improving.

CASE II.—(A72332.) P. H. G. Female, aged twenty-eight. Examined in the Mayo Clinic August 19, 1912. In June, 1911, the patient had a mastoid operation on the right side. Five weeks

Fig. 162.—(A72332.) Patient at rest, showing face filled out on affected side and no deformity except eye open wider.

later a second operation was performed, followed by complete facial paralysis on the right side.

Operation.—On August 23, 1912, the distal end of the facial nerve was severed at its exit from the stylomastoid foramen, and sutured end to end to the main trunk of the spinal accessory. The anastomosis was covered with a section taken from the facial vein.

In a letter written January 24, 1913, a little less than four and one-half months from the time of operation, the patient stated that the only motion noticed for several days was that the corner of her mouth pulled back when she raised her right arm. At the present time, five months after the operation, she can retract the corner of her mouth without moving her arm and is able partially to close her

Fig. 163.—(A72332.) Patient smiling. Note some atrophy of neck muscles due to sectioning spinal accessory nerve.

eye. I examined this patient in June, 1914. The accompanying photographs illustrate the amount of regeneration and the use of the facial muscles (Figs. 162–166). She is still improving, and I believe that the function will eventually be restored without any associated movements, since these are growing less as time goes on. There is some soreness and very slight disability in the use of the arm, but this also is rapidly disappearing.

CASE III.—(A80021.)   R. G.   Female, aged twenty-six.   Examined at the Mayo Clinic February 14, 1913.   This is an interesting case because the patient had an aneurysm, probably of the lateral sinus of the right side.   For six years she had been deaf in her right ear, which had discharged continuously, with, at intervals, severe

Fig. 164.—(A72332.)   Forcible closure of eye on affected side and contracture of facial muscles, showing nearly normal function.

hemorrhage.   There was a pulsating tumor an inch in diameter in the parotid gland, just in front of the external auditory meatus, due to an aneurysm of the facial artery.   She also had an aneurysm of the internal carotid artery on the left side of the neck, just below the angle of the jaw, producing a pulsating tumor two inches long by an inch in diameter.   Right facial paralysis had existed for five

Fig. 165.—(A72332.) Showing normal use of arm after spinal accessory nerve sectioned.

Fig. 166.—(A72332.) Showing slight associated movements of facial muscles when abducting arm.

years since an operation for a growth in the right auditory canal. Patient thinks she has never closed her right eye since childhood.

Operation.—On February 26, 1913, the external carotid artery and the internal jugular vein on the right side were ligated, as well as the common carotid artery on the left side, just below the bifurcation, and also the external and internal jugular veins on the left side. The patient had an uninterrupted convalescence from this procedure, and on May 12, 1913, an anastomosis was made between the distal end of the facial nerve, which was severed at its exit from the stylomastoid foramen, and sutured end to end to the main trunk of the spinal accessory. On February 4, 1914, nearly nine months after the operation, the patient writes that, in the morning on arising, she notices that she can close the right eye the same as the other, and that there is a little movement on the right side of the face when she talks. Since this time she has made progressive but slow improvement. The associated movements between the arm and face in this case have never seemed to be at all marked, and she has perfect use of her arm, except that there is some soreness present.

CASE IV.—(A113147.) E. G. Female, aged forty-six. Examined August 31, 1914. Patient had been operated on July, 1904, for acute mastoid trouble. A second operation was performed five weeks later, and, following this, there was complete facial paralysis on the right side.

Operation.—On September 3 the spinal accessory and the facial nerves were anastomosed. The anastomosis was covered with a section taken from the facial vein.

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CYSTIC ODONTOMAS*

GORDON B. NEW

The subject of cystic odontomas has not received in this country the same study that it has in England, Germany, and France. The importance of the subject is readily appreciated when one considers the marked deformities of the face and jaws that accompany these growths, which early diagnosis and thorough operation might have eliminated in many cases.

Cystic odontomas will be considered under two classes—the simple cysts and the adamantinomas. The simple cysts are again divided into two types: Type A, including the cysts commonly called dental or root cysts, and Type B, those usually called follicular cysts and containing a partially formed tooth. The term "follicular cyst," used for the second type, is misleading in that one takes for granted, without knowing definitely, that this type is developed from the follicle of a tooth. The term dentigerous cysts is used quite loosely and may refer to either of the above types of simple cysts. For this reason it has not been used in my classification.

Twenty-six cystic odontomas are herein reported from the Mayo Clinic. Twelve of these are simple cysts of Type A; 6 are of Type B; and 8 are adamantinomas.

The simple cysts (Type A) are the most common cysts of the jaws. Because of their little surgical importance, they have not received the attention which has been given to other cystic odontomas. Magitot,[1] in 1872, published the first important work on the subject of cystic odontomas and attributed their origin to the

development of the embryonic dental tissue. Malassez,[2] in 1885, found masses of cells about the roots of teeth in the jaws of adults and concluded that these were the remains of the dental ridge, the epithelial cord, and the outer layer of the enamel organ. These cells may be found near the teeth, and are sometimes found deep in the jaws. Malassez called these masses of cells, "débris epithéaux dentaries," and proposed the theory that all cystic odontomas were derived from this group of cells. This theory is the one most commonly accepted.

According to Scudder,[3] this type of cyst is found more commonly in the upper jaw, in the incisor and bicuspid regions. Of the 12 cysts of this series, 6 occurred in the upper jaw and 6 in the lower. Of those in the upper jaw, 4 occurred in the incisor region, 1 in the bicuspid region, and in one case the location was not noted. In the lower jaw 3 occurred in the incisor region, 2 in the bicuspid region, and one in the molar region.

The typical mammalian dentition consists of 44 teeth, and man has but 32, a third incisor, a third bicuspid, and a fourth molar being missing. The most frequent location for the appearance of supernumerary teeth is in the upper jaw, in the incisor and bicuspid regions. Whether these teeth are a reversion to the earlier types in the mammalian dentition or simply mishappenings is a questionable point among those who have made a thorough study of the subject. It is interesting to note that this type of cyst and the supernumerary teeth most frequently occur in the same location, which might suggest that these cysts are derived from supernumerary anlagen.

The theory has been held for some time that these cysts develop from irritation or stimulation. The irritating factor may be the eruption of a tooth or some form of peridental inflammation. These cysts are frequently found in connection with the dead roots of teeth, and thus the irritative factor necessary to stimulate their growth is accounted for.

Simple cysts of Type A occur at almost any age. Of the 12 cases reported in this paper, the youngest patient was twelve years of age and the oldest seventy. The cyst is usually about the size of an

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English walnut, but may attain great dimensions, and in the upper jaw simulate an empyema of the antrum. In the lower jaw it may become as large as an orange. The cysts from our series varied in size from that of a cherry to that of a small lemon. Witzel[4] found tumors the size of a pea and smaller about extracted teeth. They were placed sometimes near to and sometimes distant from the root of the tooth. They contained fluid and had an epithelial lining
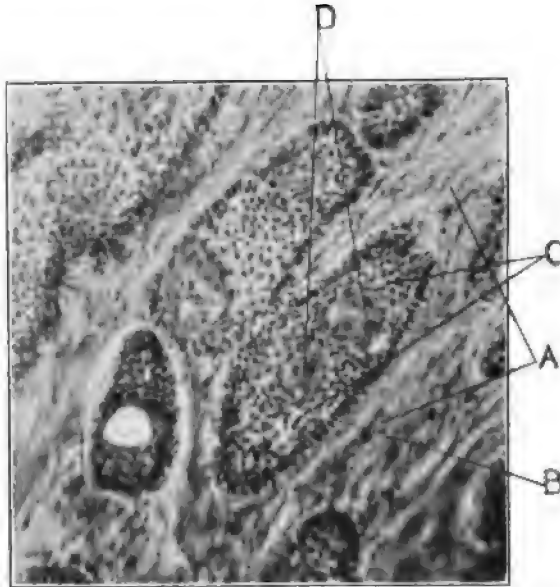
Fig. 167.—(A68435.) *A*, Connective-tissue stroma; *B*, columnar epithelium; *C* and *D*, differentia cells; *B*, *C*, and *D* are analogous to the cells of the enamel-organs.

indistinguishable from a larger cyst. The cysts have a smooth mucous membrane covering in the mouth; the wall varies in thickness and consists of a thin shell of bone (Fig. 167).

CYST (TYPE B)

Malassez[2] believes that this type of cysts also originates from cells that he describes in the jaws. Bland-Sutton,[5] however, believes that this type simply represents an expanded tooth-follicle.

These cysts occur in either jaw with about equal frequency, and usually in the bicuspid and molar regions. Of the 6 cases in our clinic, 3 were found in the upper and 3 in the lower jaw. Of the 3 in the upper jaw, 1 occurred in the bicuspid region, 1 in the molar region, and in 1 case the location was not noted in the history. Of the 3 in the lower jaw, 1 occurred in the bicuspid region, 1 in the anterior part of the jaw, and 1 in the molar region.

This type of cysts occurs during or shortly after the second dentition, except those in connection with the third molar, which

Fig. 168.—(A59772.) Adamantinoma. Early cyst formation by the disintegration of the differentiated cells.

develop later in life. Although this fact is commonly known, this type of cyst may not cause symptoms or be noticed until later in adult life. Of our cases, other than those in which the cyst occurred in the third molar region, the ages of the patients were three, fourteen, and twenty-eight years; of those in the third molar region, the ages were twenty-seven, thirty-four, and thirty-seven years.

It is noted that a tooth is missing from the set, and a partially developed one found in the cavity of the cyst. The crown of the

tooth is usually complete, and the root partially formed.   These
cysts occur about a partially developed permanent tooth, and are
rarely seen about a supernumerary tooth.

In one of our cases the cyst occurred in a man sixty-nine years of
age.   He had had a tumor of the lower jaw near the angle for forty-
two years, and during the last six months it had increased in size,
and the surface had become ulcerated in the mouth.   The roent-
genogram showed a cyst with a partially developed molar tooth.
A specimen from the growth, on microscopic examination, proved
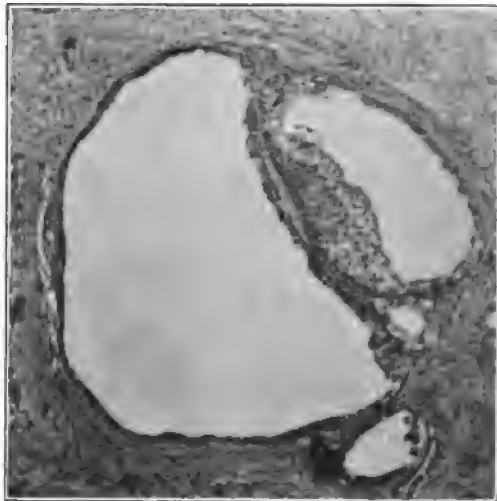
Fig. 169.—(A68435.)   More advanced stage in formation of a cyst.   Very few differentiated cells are
left.   The cyst is lined by a layer of columnar cells.

to be epithelioma.   The extensiveness of the growth and the glan-
dular involvement made the condition inoperable.

This type of cyst has characteristics of size similar to cysts
of Type A.   The wall consists of thin bone, and the mucous mem-
brane covering in the mouth is quite smooth (Figs. 168 and 169).

ADAMANTINOMAS

The adamantinomas, on account of their greater surgical im-
portance and their interesting features pathologically, have given

rise to more study than the other types of cysts. Falkson,[6] in 1879, held that, in the formation of enamel organs for the several teeth, there was a surplus of those formed, and that these additional dental germs were the origin of the adamantinomas. Malassez's theory as to their development from the epithelial masses found in the jaws is accepted by most observers. Kruse[7] agrees with Malassez as to the origin of the cysts, and reports 3 cases,
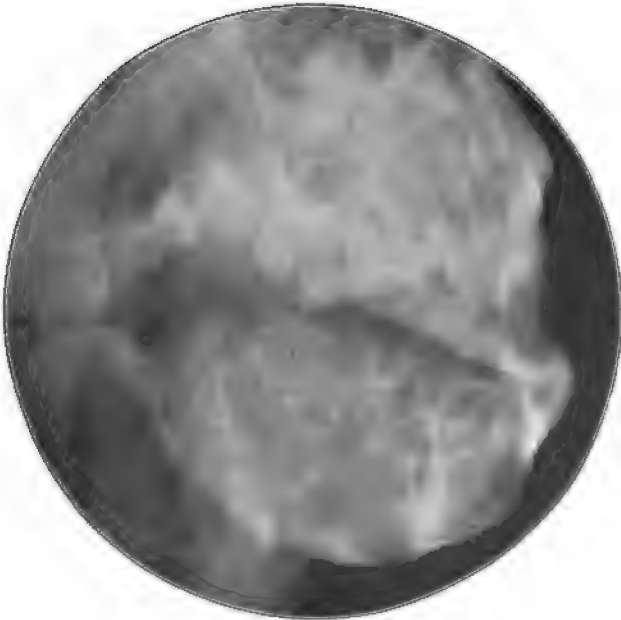
Fig. 170.—(13523.) Adamantinoma in woman, aged twenty-two. Duration of tumor, eight years Tumor involving left half of lower jaw.

each one typifying different stages in the development of the cells of the enamel organs. Büchtemann[8] and Kolaczek[9] believe that these tumors originate from the mucous membrane or from the mucous glands of the mouth. Bland-Sutton[5] and others hold that they are formed from the oral mucous membrane. Bland-Sutton's argument against Malassez's theory is that they occur in middle life and that if they were derived from the embryonic enamel organ,

they should occur at an earlier period in life. Hesse[10] agrees with Falkson[6] as to the origin of these tumors from a surplus of enamel organs.

The adamantinomas are most frequently seen in the lower jaw. Lewis[11] states that they are seen 11 times more frequently in the lower than in the upper jaw. The bulk of the tumor-mass is usually at the angle of the jaw, extending upward to the ramus and

Fig. 171.—(13523.) Same case as Fig. 170, showing transplanted rib in place after resection of tumor by Dr. Judd. Transplant healed nicely.

forward into the body of the jaw. Sometimes the entire ramus is cystic, with the tumor extending across the midline to the other side of the jaw. These tumors may originate in the molar or bicuspid regions, but are rarely seen originating from about the anterior teeth (Figs. 170 and 171).

I have been able to collect 9 cases in which the tumor occurred in the upper jaw, 2 from the Mayo Clinic. In only 4 of the cases

reviewed in the literature were there definite data as to the location in the jaw. Four of the 9 occurred in the posterior part of the jaw, and 2 in the cuspid region. These cysts may originate close to the alveolar border, or may start from deep within the jaw. Of the 8 cases of adamantinomas from our clinic, 6 occurred in the lower jaw and 2 in the upper. Of the tumors in the lower jaw, in 4 the main mass was located in the angle of the jaw, in 1 in the molar region, and in 1 in the bicuspid region. Of those in the upper jaw, 1 occurred well back in the molar region and 1 in the cuspid region (Figs. 172 and 173).

Fig. 172.—(A89376.) Adamantinoma. Woman, aged fifty. Duration of tumor, twenty-one years.

These cysts may develop at any age. Massin[12] reports a case in a new-born infant, and cases have been reported late in adult life. Lewis[11] states that the average age of the patients in the 70 cases which he collected in the literature was 33. The average age of the patients in our group of cases is twenty-seven and one-fourth years. Of the 6 cases from the literature in which the tumor occurred in the upper jaw, the average age of the patients with occurrence in the molar region was thirty-three and one-half years, and of those with occurrence in the cuspid region, sixteen and one-half years.

Stumpf[13] says that if either of the theories which have been
advanced for the etiology of the formation of these cysts is accepted,
one must assume some additional irritant factor as necessary in
their production.   The lower molar region receives more irritation
than any other locality in the mouth.   It is an accepted fact that
the lower third molar is more difficult to erupt and more frequently
impacted than any other tooth in the mouth.   It is interesting to

Fig. 173.—(23705.) Roentgenogram of case in Fig. 172, showing entire absence of ramus of jaw on
right side and the tumor extending across midline to bicuspid region on left side.

note that it is in this region, and at the average age of thirty-three
years, during or just at the time of the eruption of the lower third
molar, that these cysts occur; and also that, of the cases in the
literature in which the upper jaw was affected, the average age of
the patients having adamantinomas in the molar region was thirty-
three and one-half years, while that of patients with involvement of
the cuspid region was sixteen and one-half years.   This suggests

that the eruption of the teeth may play an important part in the chronic irritation, which is probably necessary to stimulate the growth of these tumors. If these conditions develop from super-numerary anlagen, the different locations in the molar region may be explained by the fact that, according to Black,[14] the super-numerary molar tooth may occur in any location posterior to the
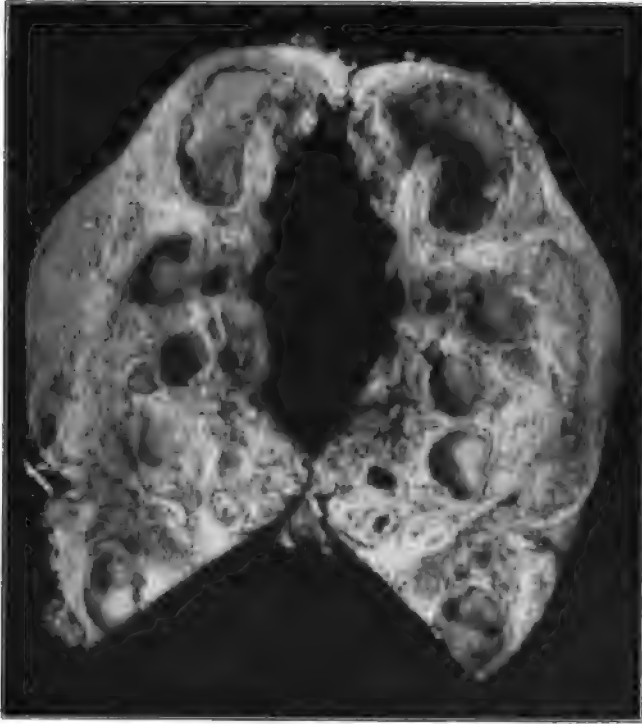
Fig. 174.—(A59772.) Adamantinoma. Cross-section, showing the solid areas of the tumors and the small and large cysts with bony walls.

first molar. The adamantinomas are sometimes associated with cysts containing partially formed teeth, but not frequently enough to make this a factor in the etiology.

It is difficult to obtain conclusive evidence of the association of the eruption and impaction of teeth to adamantinomas, as most histories are not of sufficient detail on this point. Hesse,[10]

in 1912, reported a case in which a lower third molar was found in connection with an adamantinoma, and believes that from a study of this case he will be able to find out more about these tumors. Two of the adamantinomas in our clinic were associated with unerupted third molars, one in the upper and one in the lower jaw (Figs. 174 and 175).

Of the 70 cases that Lewis collected from the literature, the average duration of symptoms was eight and one-half years. The duration of the symptoms in our cases was from ten months to
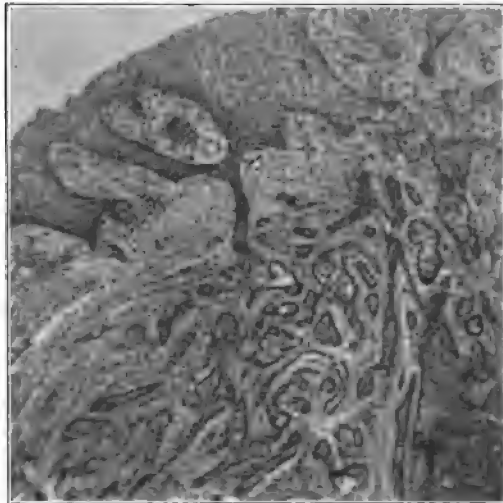
Fig. 175.—(A68435.) Adamantinoma. Down-growth of the columns of epithelial cells and the various forms these take, surrounded by connective-tissue stroma.

twenty-one years. Most of the cases were of more than ten years' duration. However, the exact duration of these tumors is difficult to determine on account of the long standing of the condition.

In none of the cases reported in this paper was there any glandular enlargement. Two cases have been reported recently in the literature which had metastases in the neck from adamantinoma.

These tumors present a smooth mucous membrane in the mouth unless they are infected. The wall of the cyst is comprised of a thin layer of bone. Crackling may be elicited in some areas,

on pressure, where the bone is thin, and fluctuation may be found in others. These tumors may give rise to great pain when they are of large size, due to pressure of inclosed fluid. One of our patients who had had a tumor for twenty-one years, in order to relieve the pain, had for some years tapped the cyst herself, by means of a sterilized hat-pin, as the fluid accumulated.

Pathology.—The lining of the simple cyst, Type A, consists of a layer of fibrous tissue and a thin layer of flattened epithelial cells. In the older cysts this latter layer may not be present, probably due to the pressure of the inclosed fluid. Barrie,[15] in 1905, reported a case of dentigerous cyst which was probably a simple cyst, Type A, with typical adamantine epithelium, with no downgrowth, lining the cyst. This was the first case reported with this type of epithelium forming the wall of the cyst.

The lining of the simple cyst, Type B, consists of a fibrous tissue layer. Some observers have reported an epithelial lining for this type of cyst also.

The adamantinomas on section present solid and cystic areas. The cystic areas vary in size from that of the head of a pin to that of an English walnut. They appear to have a smooth lining, and fibrous or bony septa are seen separating the various cysts. The cysts contain a thin yellowish fluid. The solid areas have a red tint, and present a granular appearance due to the many minute cysts.

Microscopically, the solid areas consist of a fibrous tissue stroma and columns of epithelial cells. These columns may be elongated, rounded, or arranged in the form of acini, and may present many irregular forms. Two types of epithelial cells are found in these cell columns: the typical columnar cell with the nucleus placed near the pole away from the stroma, and the differentiated cells from this type—the polygonal cell and a stellate cell which form the main mass of the epithelial columns. These cells are analogous to the cells that form the enamel organ. Areas of transitional forms from the solid cords to the small cysts are seen. The stellate cells are seen undergoing disintegration, and their place being taken by cyst cavities, at first quite small and then

becoming larger. Stellate cells gradually disappear and are re-
placed by the fluid of the cyst. As the cyst increases in size the
columnar cells are alone left to line the cyst, while in the yet larger
cysts these have disappeared and the wall consists of fibrous tissue
only.

Diagnosis.—The diagnosis of the cystic odontomas, when the
facts already noted are considered, and with the aid of the roentgeno-
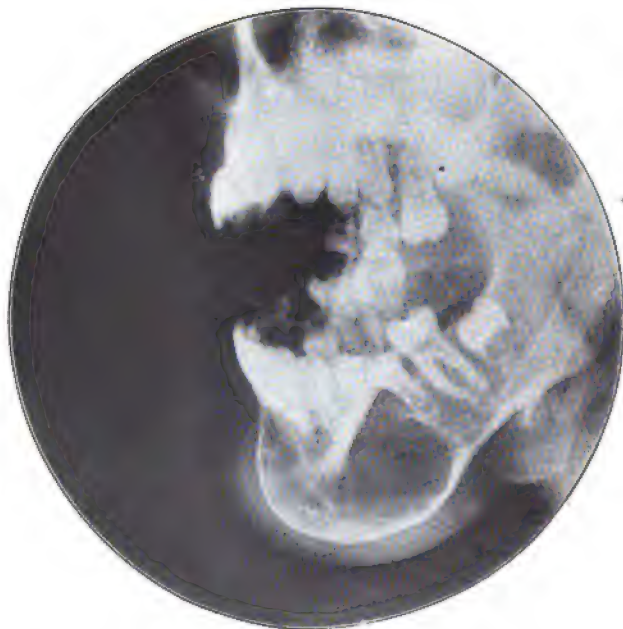
Fig. 176.—(12017.) Girl, aged ten. Duration, four months. Simple cyst, Type A, involving anterior
of lower jaw.

gram, is usually not difficult. The roentgenogram will show a
partially developed tooth, a unilocular cyst, or the septa in the
multilocular variety. The differential diagnosis from a giant-
cell sarcoma is usually the most difficult, and this has frequently
to be made at the time of operation or by microscopic examination.

Treatment.—The treatment of the cysts of the first group re-
quired only a thorough cureting of the wall and packing the cavity

with gauze. In the larger type, resection may be required to extirpate the tumor. The adamantinomas, however, require more radical treatment, since the simple cureting of the cyst does not permanently cure the condition if a small area of the tumor is left. In time the condition recurs. A resection of the jaw should be

Fig. 177.—(A 29772.) Adamantinoma. Gross specimen.

made, if possible; in this way all the tissue of the tumor may be removed. Different appliances have been used, including metal splints to hold the fragments of the jaw in position after resection, but the transplantation of a portion of rib seems to be the most satisfactory (Figs. 176 and 177).

Recurrences are frequently noted in these tumors, especially when the treatment has been conservative. Bloodgood[16] reports 12 cases of adamantinomas. One case was inoperable, and in 11 cases resection of the jaw was done. Nine of these patients were well from one to twelve years. There was one recurrence after the patient had been well for eight years. One died following excision of a huge tumor involving both sides of the upper jaws.

Of the 8 cases reported from our clinic, all the patients have been operated on within the last two and one-half years, so that the final results cannot be given. One patient died of heart trouble eight months after the operation, and two have been operated on within the last six months. In one case the tumor recurred, but the patient has now been well more than two years; one recurred after two years and the patient has been reoperated on for the recurrence within the last six months. In one case, on account of the extensiveness of the tumor and the fact that the cyst consisted of fibrous walls which involved the entire half of the jaw and the ramus and extended across the midline, resection was impossible. The tumor was opened and the cysts cureted. Several small cysts have appeared since the operation. Two patients have had no recurrence—one case is of eighteen months' and one of two years' standing.

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CONGENITAL DIAPHRAGM OF THE LARYNX*

GORDON B. NEW

According to Thomson,[1] there are but 20 cases of congenital diaphragm on record. The first case was reported by Turhelle[2] in 1869.

I wish to report here the history of a patient who was examined in the Mayo Clinic on July 16, 1914.

Fig. 178.—Shows congenital diaphragm of the larynx. The mesial margin of the anterior two-thirds of the true cords is joined by a thin triangular membrane.

CASE 110482.—E. B. G., male, twenty-seven years of age. Well developed and healthy. No family history of similar conditions. No history of any acute condition of the upper air-passages. There had been a hoarseness from birth, with no apparent change in the voice. The patient had slight difficulty in breathing on exertion, as in running upstairs. Examination of

the larynx showed a thin membrane extending between the margins of the true vocal cords for two-thirds of their extent anteriorly, with a clean-cut concave margin toward the lumen of the glottis. The membrane was pale gray in color, gradually fading into the margin of the cords, which were rounded and slightly reddened. The membrane appeared thinnest in the median line and at its free margin. It did not present an appearance of scarring, and the larynx was otherwise quite normal. During phonation the membrane between the cords almost completely disappeared, although enough remained to prevent the approximation of cords. In the examination of the eyes, ears, and nose no other abnormalities were found; Wassermann negative. The diagnosis of congenital diaphragm of the larynx was made because— (1) The history of hoarseness since birth; (2) the absence of any previous illness which might cause such a condition; (3) the appearance of the diaphragm and the otherwise normal larynx.

Operation.—With a laryngeal knife the diaphragm was split down the center from the free margin to the anterior commissure. As the knife approached the anterior commissure it met with marked resistance on account of the increase in thickness of the membrane. Although measures were taken to prevent it, adhesions of the cords at their anterior part occurred. After reaction from the operation had cleared up, the patient's voice became slightly improved, and he noted that he could breathe with greater ease.

Etiology.—Ganghofner[3] shows that the laryngeal anlage consists of two ridges symmetrically placed, which bound a small fissure. These ridges, which later form the walls of the larynx, lie close to each other, and at a certain stage of development are attached by epithelial adhesions or agglutinations. In 1878 Roth[4] brought out the fact that the persistence of these epithelial adhesions between the cords was the cause of congenital diaphragm of the larynx. Scheff[5] was the first to explain that congenital diaphragm was due to the persistence of embryonal adhesions. Fein[6] holds that the epithelial adhesions are due to the thickening of the laryngeal walls, consisting of mesenchyme without much lateral growth. The lumen of the laryngeal anlage is thus partially obstructed, and epithelial adhesions are formed. He finds that this begins about the end of the first month of fetal life. The sepa-

ration of the laryngeal walls is apparently due to the expansive growth of the larynx. Lewis,[7] in a study of the embryology of the larynx of the fetal pig, agrees with Fein as to the production of the concrescence. He states in his conclusions that the concrescence is dependent on the rapid growth of the mesenchyme of the laryngeal anlage which compresses the less resistant epithelium. The beginning of the solution of the concrescence is coincident with the differentiation of the mesenchyme of the laryngeal anlage into cartilage and muscle.

Hereditary influence also seems to play a part in this condition. Siefert[9] noted that the father and sister of a patient had similar formations of the larynx, while Glas[8] noted that the mother of a patient with diaphragm of the larynx had apparently congenital adhesions between the margins of the cords at the anterior commissure. Fraenkel[10] also found a rounding of the angle at the anterior commissure in the mother of a patient.

The association with this condition of another congenital deformity in the same patient has been found by various observers. Glas[8] found shortening of the frenum linguæ in one, and Imhofer[11] found a coloboma of the upper lid associated with the congenital laryngeal diaphragm. This would seem additional evidence that the diaphragm is a congenital condition. Hanseman[12] and others believe the diaphragm is due to an inflammatory condition occurring in utero, but this theory would seem to be discredited by the microscopic examinations of the diaphragm, which does not show scar tissue, but tissue similar to that of the cords. Scars from syphilis, tuberculosis, or rhinoscleroma should be considered in the diagnosis, especially in older individuals, since similar pictures are seen in the scarring of the larynx in later life.

Harmer[13] and Glas[8] have demonstrated the condition to be congenital by microscopic examinations of the diaphragm. Their sections showed tissue containing mucous glands and musclefibers. Flat epithelial cells were present on the upper surface, and cylindric epithelial cells on the under surface, similar to the cords. No scar tissue was found.

The congenital diaphragm of the larynx is usually in the ante-

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rior part of the larynx. According to Harmer,[13] only two cases have been reported in which the diaphragm was in the posterior part. The membrane occurs between the posterior margins of the vocal cords and gradually loses itself in the interarytenoid mucous membrane. The diaphragm of the anterior part of the larynx may vary in size from a simple rounding of the angle of the anterior commissure to the size of the one reported in this paper. The rounding of the anterior commissure is not an infrequent finding in the examination of the larynx, and most observers believe that the etiology of this condition is similar to that of the diaphragm of the larynx. Small membranes have been seen in the anterior part of the larynx in the subglottic region, and not in any way connected with the cords.

Results of the treatment of these conditions have, as a rule, been unsatisfactory because the raw surfaces of the anterior commissure heal together. Improvement in the voice is not usually marked, although the patients notice the increased ease with which they breathe.

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CLINICAL AND RADIOLOGIC FINDINGS IN PULMONARY TUBERCULOSIS*

The Value of a Coöperative Diagnosis

HERBERT Z. GIFFIN AND WALTER D. SHELDON

Scientific investigation demonstrates that tuberculosis is well-nigh universal in modern life. Our presence here to-day is sufficient evidence that nature has endowed us with an admirable system of defense. The prevalence of tuberculosis results partly from our ignorance and partly from our inability to apply the knowledge that we possess, while the failure of the natural defenses in many instances is due to causes over which the medical profession has little control and to which it has given little attention.

From the earliest time the consumptive has been recognized by his associates, but it has been only since Laennec and Auenbrugger that methods of diagnosis have become known which develop the local signs of disease. "Early tuberculosis" has always been a relative and *progressive* term. The failure to recognize early tuberculosis rests primarily with the patient, but the medical profession must bear a large measure of this responsibility because of negligence, defects in our methods of education, and the many obstacles met with in private practice. Thus far the duties of the medical profession have been to determine the presence of the disease in those who solicit their opinion, though in the army, navy, and in some other organizations a satisfactory state of health is a requirement. The indifferent, the thoughtless, and the ignorant may come to recognition late and consequently spread the infection for years.

The rapid growth of specialism within recent years furnishes abundant evidence that none of us is able single-handed to make a practical application of scientific medicine. With specialism arises also the necessity for coöperation, which, it is true, as yet is attained with considerable difficulty and expense. Even in the hands of the most skilful, the diagnosis of pulmonary tuberculosis has dangerous limitations. Cases with obscure signs leave both patient and physician in a state of anxious perplexity. The specialist and the internist are, therefore, the first to appreciate any assistance that can be rendered by laboratory methods, and are especially interested at the present time in a determination of the relative value of the roentgen-ray in the diagnosis of pulmonary tuberculosis.

Eisler,[1] Sluka,[2] and Rach[3] have published exhaustive discussions concerning tuberculosis in children. The x-ray has been the means by which the time of onset, the location, the extension, in a word, the entire course following a primary infection of tuberculosis in children, has been studied. Owen and Morton[4] have presented contributions from the clinical standpoint, while Jordan,[5] Dunham,[6] Moore,[7] and others have presented the technical and laboratory phases of the work.

A consideration of the subject classifies itself under two headings: (1) The value to the clinician of a positive x-ray diagnosis and (2) the value of a negative diagnosis.

THE VALUE TO THE CLINICIAN OF A POSITIVE DIAGNOSIS BY THE ROENTGENOLOGIST

The relative value of the study of stereoscopic plates of the chest as an aid in the diagnosis of pulmonary tuberculosis will naturally vary with many factors. The skill with which Roentgen plates are made, the conservatism and the experience of their interpreter, on the one hand, and the skill of the internist, the degree of care in searching for physical signs, and the length of time during which a patient may be under observation, on the other, will cause a great variation in the esteem for roentgenology in different clinics.

We can, however, in a discussion of this character, depart from common ground. While a highly presumptive diagnosis of pulmonary tuberculosis may be based upon definite signs alone, nevertheless the only absolute proof of a positive diagnosis is the finding of the tubercle bacillus in the sputum. In a series of 373 patients with tuberculosis of the lungs observed between July, 1913, and June, 1914, 194 showed positive sputum. Of the 194, 177 were rayed. In these 177 cases with positive sputum that were rayed an *independent* x-ray diagnosis was given. This diagnosis was based on a study of stereoscopic plates. In every instance save one the x-ray diagnosis was positive for tuberculosis. We can, therefore, assert with some degree of finality that practically every case of pulmonary tuberculosis in which tubercle bacilli are found in the sputum will show positive findings on a proper Roentgen study.

Recent cases have been used in this study in order that we might avail ourselves of the increased experience and skill of the roentgenologist, and the keener interest and more careful work on the part of the clinician which have naturally resulted from the several previous years of attention.

Of the 373 cases, there were 142 positive x-ray diagnoses in which the sputum, if any, was negative. In these instances the diagnosis by clinical methods is, of course, not conclusive, because of the fact that healed tuberculosis and early tuberculosis and lesions centrally located may give no signs, while diffuse and miliary tuberculosis may produce very indefinite findings. A review of the histories, however, almost always corroborated the Roentgen findings.

The one case mentioned above in which the sputum contained tubercle bacilli and in which the x-ray findings were negative is worthy of discussion. This patient was a girl aged twenty-four years, who gave a three-year history of complaint. Long periods had been spent in bed; cough and fever had been present at times. She had raised several mouthfuls of blood. For three years the pulse-rate had been rapid, the rate frequently reaching 120. An enlargement of the thyroid had been noticed for two years, to-

gether with weakness, nervousness, tremor, and dyspnea.   Tubercle bacilli had formerly been found in the sputum.   Recently there had been a gradual gain in weight up to 195 pounds.   Absolutely no signs were noted on examination of the chest, while the x-ray plates showed only bronchial thickening.   It may be possible that this case was not one of pulmonary tuberculosis, but rather of hilus tuberculosis.   The possibility of a tuberculous bronchitis must also be considered.

It was formerly believed and stated that radiography would never reveal a lesion that could not be found by the internist, provided a reasonably thorough and prolonged observation of the patient were made.   This we believe has been disproved.   We have studied our cases with respect to the physical signs, the clinical history, and the probability of a diagnosis without the x-ray findings, each of these on a basis of 4—4 representing a diagnosis made positive by the finding of the tubercle bacillus.   Of 154 cases in which tubercle bacilli were not found, there were 30 in which the probability of a diagnosis upon clinical findings alone was extremely small (degree 1), and 20 in which a diagnosis seemed entirely impossible.   This latter group of 20 in which a diagnosis was impossible includes early cases, healed cases, and diffuse tuberculosis.

Another question naturally arises, "Will the roentgenologist make a diagnosis in early lesions?"   It should be emphasized that the diagnosis depends on the interpretation of the plate.   The roentgenologist, not the x-ray, makes a diagnosis.   Moreover, as has already been noted, an "early lesion" and an early diagnosis are purely relative terms.   It must be determined what constitutes an early diagnosis.   Does it depend on the duration of the history or on the extent of the lesion?   Doubtless "early," as we understand it at present, infers a consideration of both these factors, while the duration of definite symptoms is the more important of the two.   There has been a constant inclination in our attempts at making an early diagnosis to fall into the error of ascribing a few signs at the apex of the lung to tuberculosis, especially in the individual who is neurasthenic or debilitated.   But these findings are only presumptive evidence of tuberculosis.   Apical signs without

tuberculosis occur most frequently in children, and occasionally in an adult a localized apical bronchitis is quite apt to occur, especially in association with nasal affections. These patients will naturally improve on fresh air and constitutional treatment, and may be classified falsely as "cured" cases of tuberculosis. The question capable of proof is this, "Are there cases showing positive sputum and the signs of an early tuberculosis that are negative upon x-ray examination?" One hundred and ninety-four cases of our series gave positive sputum. Of these, 177 were rayed, and no case that could be classified as an early tuberculosis was found in which the x-ray report was negative. The one patient cited above in which tubercle bacilli were present and the stereoscopic plates were negative cannot be grouped with the early cases, as the duration of the history was three years. Of the above series, 24 can be regarded as so-called early cases from a consideration of the history and findings.

This conclusion does not infer that a lesion cannot be so early that neither the physical examination nor the Roentgen examination may not fail in a diagnosis, but deals only with the relative value of the x-ray in those early cases in which there is positive sputum. An opinion concerning the value of roentgenology in the diagnosis of those early cases of pulmonary tuberculosis in which the sputum has been negative must necessarily await a knowledge of the subsequent histories in large series of cases with negative plates. Certainly it would seem at the present time that an examination of stereoscopic plates of the lungs by a skilful operator and interpreter is most trustworthy evidence in the diagnosis of early tuberculosis. It is to be hoped, however, that some day we may make a diagnosis of tuberculosis earlier than is at present possible.

An occasional case suggests a probable diagnosis of tuberculosis when the sputum and ray are negative. Two cases of this type are included in the series. In one of these, a girl of fourteen, there had been cough for six months, but no sputum. Two hemorrhages, however, had occurred in the last two months. The physical signs were so indefinite as to be practically negative. In the other case, a woman of twenty-seven, there was a history of pleurisy seven

years previous, and this was followed by cough, sputum, and night-sweats.   The patient came to a physician because of gastric symptoms, slight cough, and expectoration.   A few fine crackles were heard over both apices, while the breath-sounds were harsh over the left upper lobe.   Examination by x-ray, however, was negative.

Possibly the most interesting assistance that has been obtained as one looks back over his experience consists of the visualization of our suspicions as they are revealed by the radiogram.   The development of a keener sense of perception has followed the corroboration of our findings when shown graphically on the plate.   Many failures in diagnosis have occurred, and roentgenology has really been a stimulus to physicians to perfect their skill at physical diagnosis that they may not lose their proper place in the scheme for coöperative laboratory and clinical conclusions.

The Roentgen ray in almost every instance shows a more extensive lesion than was suspected by physical examination.   It may, therefore, be of considerable value from a prognostic standpoint.   It also frequently shows lesions which, on account of their location, are to all other methods inaccessible.

THE VALUE TO THE CLINICIAN OF A NEGATIVE DIAGNOSIS BY THE ROENTGENOLOGIST

In the routine of general diagnosis a negative radiologic report of the lungs may be of very great value.   Further experience may show that the negative value is equally great if not greater than that obtained in a positive way.   There are certain diseases in which this has been notable in our experience:

Chronic Bronchitis, Asthma, or Emphysema.—Stoll[8] has called attention to the fact that tuberculosis in the aged has often been overlooked.   Its recognition is made difficult chiefly because of coexistent chronic bronchitis, asthma, or emphysema.   One of us (Giffin)[9] has reported cases of tuberculosis which were for years regarded as asthma.   These patients had doubtless spread the infection unwittingly.   In our series of 373 cases there were 13 in which a history of spasmodic asthma was obtained, and of these 5 showed the presence of tubercle bacilli in the sputum.   The signs

in chronic bronchitis and asthma are frequently so plentiful that they easily mask the evidence of a localized lesion.   The value of a negative ray may, therefore, be of very practical help in these cases.

Anal Fistula.—Seven instances of anal fistula in association with pulmonary tuberculosis are included in this series.   The finding of pulmonary tuberculosis generally modifies the line of treatment adopted in these cases.

Goiter.—Five patients presented themselves complaining of goiter.   Their symptoms simulated in a more or less imperfect way those of toxemia.   When weakness, nervousness, tremor, or a rapid pulse occurs in association with an enlargement of the thyroid, it is not strange that intoxication should be suspected and a more complete study be necessary before tuberculosis is recognized as the cause of the patient's condition.   In this group of cases a negative plate may be of great diagnostic help.

Neurasthenia.—It is only necessary to record the general experience that every method of assistance which it is possible to utilize is welcome in the diagnosis of neurasthenia, which must often be made by exclusion.   In great numbers of these patients tuberculosis is suspected, and among other things a radiogram is necessary to exclude its existence.

Phobia.—An occasional patient in whom there exists a true phobia of tuberculosis presents himself, and we cannot deny the assistance from the psychic effect that can be had by an assurance that every method of examination has shown negative results.

Meningitis.—The roentgenologist may assist in the diagnosis of the type of meningitis which is present in a given case.   We have been able to recognize tuberculous meningitis by the assistance of positive findings in the radiogram when the physical signs were otherwise indefinite.

Subinfections.—The so-called subinfections, in which there is an occasional rise of temperature, have been very puzzling from the standpoint of diagnosis, and it might be said that the roentgenologist's opinion is essential in order to assist in excluding active pulmonary tuberculosis.   In these cases, if evidence of tuberculosis be

entirely lacking, we may then without delay proceed in the search, generally a difficult one, for some focus of infection.

Obscure Symptom-complexes of the Upper Abdomen.—In the diagnosis of obscure symptom-complexes of the upper abdomen pulmonary tuberculosis must necessarily be excluded. Patients with irregular types of indigestion sometimes simulating gastric neurosis and sometimes gastric ulcer may in reality prove to be tuberculous. When abdominal symptoms simulate tuberculous peritonitis or tuberculous salpingitis, radiographic findings may be important evidence to a conclusion.

Surgical Conditions.—In certain surgical conditions the decision as to the existence of tuberculosis is frequently most important. The extent of the lesion may be a decisive factor in a consideration of the advisability of surgical treatment. Should the lesion in the lung be localized, surgical treatment may in reality be beneficial, as was the case in two patients in this series who were operated on for duodenal ulcer on the basis that improvement in the digestive capacity would increase the patient's defense against the tuberculous process.

CONCLUSIONS

This study has been undertaken in order that our experience as to the value of a coöperative clinical and radiologic diagnosis in pulmonary tuberculosis might crystallize itself. The material has been approached by the writers from the physician's standpoint, while the radiologic diagnoses were made by Moore. The conclusions have been based on recent cases in order that we might avail ourselves of the increased experience and skill of the roentgenologist, and the keener interest of the clinician which naturally resulted from the several previous years of attention.

Our review of 373 cases seems to show:

1. That practically every case of pulmonary tuberculosis with tubercle bacilli in the sputum can be diagnosed independently by the roentgenologist.

2. That in almost all those cases in which a radiologic diagnosis was positive when the sputum was negative a review of the histories has corroborated the Roentgen findings.

3. That there is a considerable number of patients in whom a diagnosis seems entirely impossible by clinical methods, although the roentgenologist reports positive findings. These include so-called early cases, healed cases, and diffuse tuberculosis.

4. It would seem that a careful study of stereoscopic plates of the chest will show evidences of tuberculosis as early as we can at present be positive of its existence by any other method.

5. That a keener sense of perception is developed through the visualization of lesions, and that roentgenology has been a stimulus to physicians in perfecting their skill for physical diagnosis.

6. That the value obtained from the negative report of a skilful roentgenologist may be of very great assistance in general medical and surgical diagnosis.

7. Finally, it should be emphasized that trustworthy conclusions can be drawn only by one who has had a considerable experience in the reading of stereoscopic plates. The roentgenologist, not the radiogram, makes the diagnosis.

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THE USE OF THE *X*-RAY IN THE DIAGNOSIS OF PULMONARY TUBERCULOSIS*

ALEXANDER B. MOORE

To Albers-Schoenberg,[1] Wolff,[2] and other European observers, and to Dunham,[3] Lange,[4] Hickey,[5] and others in this country, belongs the credit for establishing the value of the Roentgen rays to the clinician in the diagnosis and prognosis of pulmonary tuberculosis. While its importance is now almost universally admitted, its position has been rendered somewhat unstable by two factors: (1) The effervescent enthusiasm of some radiographers who insist upon the infallibility of their findings, and (2) the equal enthusiasm and confidence of certain internists who accept as conclusive the findings of their stethoscope and percussion-note in spite of all other findings.

Modern scientific diagnosis is the result of all the evidence that can be elicited by both clinical and laboratory methods, always bearing in mind the limitations of each. It is as one of the links in this chain of evidence that I would have you regard the radiographic examination.

In the examination of the lungs, as in all other branches of radiography, the success of examination depends on two primary factors—careful technic and conservative interpretation.

In the earlier days of radiography, because of the imperfections in apparatus, it was almost impossible to obtain a satisfactory radiograph of the adult chest while respiration was suspended. However, the powerful modern type of machinery and the increased

speed of the sensitive plates have largely overcome this difficulty. Perhaps the greatest advance in radiography of the intrathoracic viscera was the introduction of the stereograph.   By this method we are able to visualize the intrathoracic viscera in their true anatomic relationship and to determine on just what plane the structures showing varying degrees of density are situated.   The thorax

Fig. 179.—Chronic bronchitis.   Note the increase in the hilus shadow and thickening of the peribronchial tissues.

has been called the playground of the radiographer, for in no other location is there such opportunity for radiography.   The radiograph is a shadow picture, and the structures of the organs of the thorax, on account of their varying density, are ideally shown in it. The technic we have used is very simple, and differs but little from that described by Dunham and others.   It consists in making a pair of stereoscopic plates with the patient in the upright position

facing the plate, and the tube shifted parallel to the spine.   The
upright posture is preferred because it is easily assumed by the
patient and permits more nearly perfect relaxation and rest of the
thorax, also it does not distort the relationship of the intrathoracic
viscera.   Owing to the greater density of the posterior portion of
the ribs, it is best to have that portion at a greater distance from
the plate, therefore the plate is placed in front.   To prevent dis-
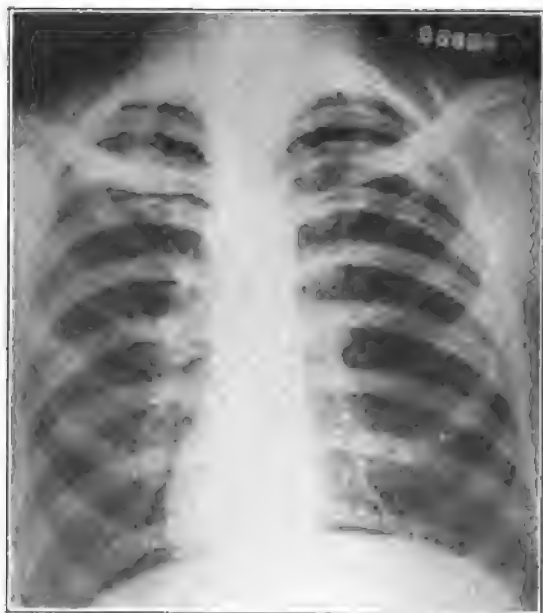
Fig. 180.—Early tuberculosis of the left apex. Note the areas of increased density just above the
left clavicle.

tortion, the distance of the target of the tube from the plate should
not be less than 30 inches.   The plate should be made with the
lungs well inflated, great care being taken to have close approxima-
tion of the patient's chest to the plate-holder and to prevent the
slightest movement while the two exposures are made.   In expos-
ing and developing plates for a study of the pulmonary tissues it
should always be remembered that we wish to preserve the softest

and less dense shadows and be careful not to obtain too dark a negative.   No radiographic examination of the lungs should be based on the study of a single plate, since it is impossible to localize a lesion in this way, hence in our work the examinations have been made routinely by the stereoscopic method.   The time required for making a satisfactory pair of stereographs should not be more than

Fig. 181.—Diffuse tuberculosis of the upper and middle right lobes.   Early involvement in the upper left lobe.

five seconds, preferably less, in order to minimize the distortion due to the movement of the heart.

In the interpretation of the radiograph we should carefully examine every detail which it contains, and always remember that shadows, not objects, are being considered.   The radiograph of a normal thorax shows the ribs, clavicles, and scapula on either side forming the bony wall;   above is the cervical spine, and below the dome of the diaphragm arching across from side to side.   In the

center is the dense shadow of the heart and mediastinum, and radiating outward on either side from this is the shadow of the hilus composed of the main bronchi and the large blood-vessels. Under ideal conditions these may be traced into five main divisions— three on the right and two on the left, corresponding roughly to the five lobes of the lungs.

Fig. 182.—Old diffuse tuberculosis involving both lungs. Note the large healed cavity in the upper left lobe and a well-marked pleuritic adhesion in the upper right lobe.

In any pathologic condition in which there is a persistent increase in the blood-supply of any portion of the lungs, with consequent thickening, areas of increased density are found in the radiograph.

From the evidence in these areas of increased density the radiographic conclusions are drawn. In inflammatory conditions affecting the main bronchi a marked increase in density of the shadow of the hilus is found. If the inflammation spreads to the smaller

bronchi, an increased density and fibrillation is found which extends outward toward the periphery of the chest, and, if consolidation takes place, definite areas of increased density are present. In examining the tuberculous chest the shadow of the hilus is increased in direct proportion to the extent of the involvement of the main bronchi, and the size of the areas of increased density correspond to the amount of consolidation, while they vary in degree of density with the stage of the disease. Early pulmonary tuberculosis gives but a faint shadow. As the process advances the density becomes greater, and, as it continues further, a cavity may form which appears in the radiograph as a clear, circumscribed area of diminished density with a dense wall. If the process is arrested and nature heals the lungs by the formation of dense scar tissue, with deposition of the lime salts, there is a still greater increase in density. It is very difficult and often impossible to distinguish by the radiograph a healed lesion from an active one, and herein lies the weakness of the radiograph. In every case of pulmonary tuberculosis there is a more or less distinctly increased density of the hilus shadow, but this same increase exists in all infectious and congestive conditions of the bronchi and lungs, hence it is of no value in determining the presence of a tuberculous lesion in the lungs. In the radiograph of practically every adult chest we find shadows of calcified glands around the larger bronchi, but it rests with the pathologist to determine whether they are due to tubercle bacilli or to some other irritant. The great number of calcified glands and the high degrees of peribronchial thickening found in coal-miners and others subjected to irritating atmospheric conditions would lead one to believe that any irritation is capable of producing this reaction.

In every case of pulmonary tuberculosis there is a certain degree of peribronchial thickening; however, an extensive simple bronchitis gives the same radiographic picture, and thus we are unable to differentiate a tuberculous from any other form of bronchitis. Since tuberculous bronchitis without pulmonary involvement is very rare in adults, we are not often confronted by this condition. In children, however, a peribronchial thickening in the absence of

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other causes should be regarded as very suspicious of tuberculosis.

From the standpoint of the radiographer the diagnosis of pulmonary tuberculosis depends, I believe, on the localization of definite areas of increased density, varying in size and degree with the stage of the disease. Of the conditions other than tuberculosis that are characterized by increased density and from which it must be differentiated those most commonly encountered are metastatic carcinoma and syphilis. In carcinoma of the lungs the areas of consolidation are more clearly circumscribed, are more massive in size, are located at the base rather than at the apex, and exhibit no tendency to cavity formation. In syphilis of the lungs the appearance is not characteristic radiographically, but is usually accompanied by a much greater thickening of the hilus than is present in tuberculosis.

From a close comparison of the radiographic findings with the clinical histories and physical and bacteriologic examinations in a large number of patients, and from the subsequent history of many, some of them extending over a period of several years, we feel that the use of the radiograph contributes very valuable information in the examination of the lungs. Its value has been especially marked in the following classes of cases:

1. Cases in which the involvement was slight and the lesions centrally located.

2. Cases in which the involvement was diffuse, both lungs being involved.

3. Cases in which the clinical picture of pulmonary tuberculosis was masked by other lesions.

4. Cases in which the clinical history suggested pulmonary tuberculosis, but the physical findings were indefinite.

In the latter type of cases we have been able, by the radiograph, to establish or disprove a tentative diagnosis of pulmonary tuberculosis, thereby rendering a negative report equally as valuable as a positive one.

This report is based on the combined clinical and radiographic findings in a series of 1000 cases of pulmonary tuberculosis which

have been examined at the Mayo Clinic during the past three years. The clinical and radiographic examinations were conducted separately, neither clinician nor radiographer having any knowledge of the findings of the other. From the radiographic standpoint the cases were classified as early, diffuse, miliary, and healed.

Early.—Twenty-four per cent. of the cases were classified as early, there being less than one lobe involved and the lesion appearing active. In 35 per cent. of these cases the lesion was situated on the right side, in 33 per cent. on the left, and in 32 per cent. both sides were involved. Clinically, 80 per cent. of these cases had an afternoon rise in temperature, and 40 per cent. of them had tubercle bacilli in their sputum.

Diffuse.—In 64 per cent. of the cases in the series more than one lobe was involved. Eighty per cent. of these cases showed tubercle bacilli in the sputum, and 90 per cent. of them showed the presence of fever. The involvement was confined to the right lung in 13 per cent., to the left lung in 9 per cent., while both lungs were involved in 78 per cent. Forty-one per cent. of these cases of diffuse tuberculosis showed the presence of cavities. Of these, 42 per cent. were situated in the right lung, 39 per cent. in the left, while 19 per cent. had cavities in both lungs. In 60 per cent. of the cases the cavities were single and in 40 per cent. multiple.

Miliary.—This series consisted of but 1 per cent. of the cases examined, all of which showed the presence of fever and none of which showed tubercle bacilli in the sputum.

Healed.—Eleven per cent. of the cases in the series were classified as healed, the lesions appearing sufficiently dense in the radiograph to indicate that they had ceased to be active. Thirteen per cent. of these cases showed lesions in the right lung, 24 per cent. in the left lung, while 63 per cent. showed lesions in both lungs. In 28 per cent. of these cases fever was present, and in 15 per cent. the sputum showed tubercle bacilli.

From a study of the foregoing cases the following conclusions may be drawn:

Conclusions

1. That the gross lesions of pulmonary tuberculosis give a characteristic appearance in the radiograph, and that the radiograph is a valuable aid in the diagnosis of pulmonary tuberculosis.

2. That the diagnosis of pulmonary tuberculosis by the radiograph must be based on the localization of definite areas of increased density, and no conclusions can be drawn from the hilus shadow in the adult.

3. That in our experience the radiograph will demonstrate any lesion the physical examination will reveal, and that in many cases, where the involvement is central, the radiographic examination will demonstrate lesions that the physical examination cannot localize.

4. That the radiograph will demonstrate much more accurately than any other diagnostic agent the extent of involvement, and that in determining the operability of a surgical condition in a patient suffering also with pulmonary tuberculosis or in giving a prognosis in a known case of pulmonary tuberculosis the radiographic examination is essential.

5. That in a large percentage of cases the radiograph cannot determine the activity of a lesion.

6. That malpositions and distortions of the shadow of the heart and diaphragm are rare, except in cases of long standing, and little or no significance should be attached to them.

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CLINICAL DIAGNOSIS OF PLEURAL EFFU-SIONS*

WALTER D. SHELDON

The physical signs upon which the diagnosis of pleural effusions rests vary considerably, depending upon the location and amount of a given effusion. Effusions may be classified as small, moderate, and large. In each group the clinical findings are quite different.

Effusions of less than 100 c.c. usually escape detection. Small effusions usually collect in the posterior or lateral aspect of the chest. In these small effusions the symmetry of the chest is undisturbed, and the range of respiratory movement is but slightly modified. The fremitus may be somewhat lessened, and the breath-sounds are slightly fainter. The most constant and reliable finding is developed by percussion. It reveals a higher position of the lower lung-border on the affected side. This deflection of the lung-border may be near the spine, but more commonly it is found in the axilla.

Moderate effusions give the classic findings when the lesion is uncomplicated. The dynamic conditions within the chest are sufficiently pronounced to produce flattening of the interspaces, fullness and partial fixation of the affected side, loss of fremitus over the effusion, absolute dullness on percussion, and diminution of the intensity of the breath-sounds. The lung-border rises to about the third rib in front and to the spine of the scapula behind. The absolute dullness coalesces with that of the heart, so that its absolute dullness, as such, is lost. Skodaic resonance is furnished

by the relaxed lung in the upper portion of the chest. So much
variation occurs in the mobility of the mediastinum that the evi-
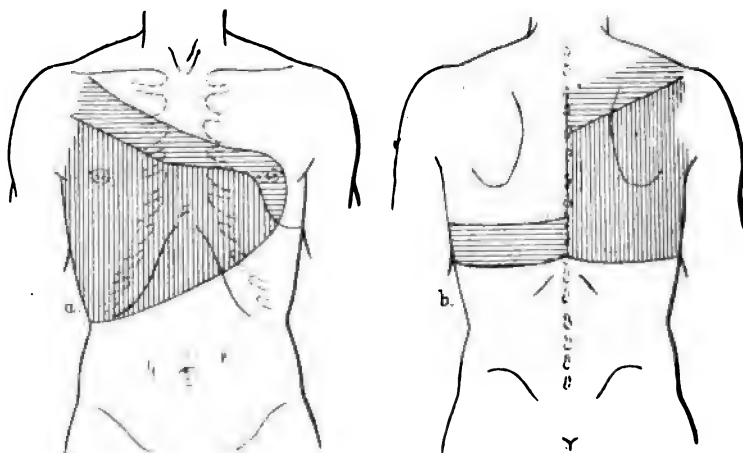
Fig. 183.—*a*, Anterior view; *b*, posterior view.   Moderate effusion.   Extension of cardiac dullness to
the left of mammary line.
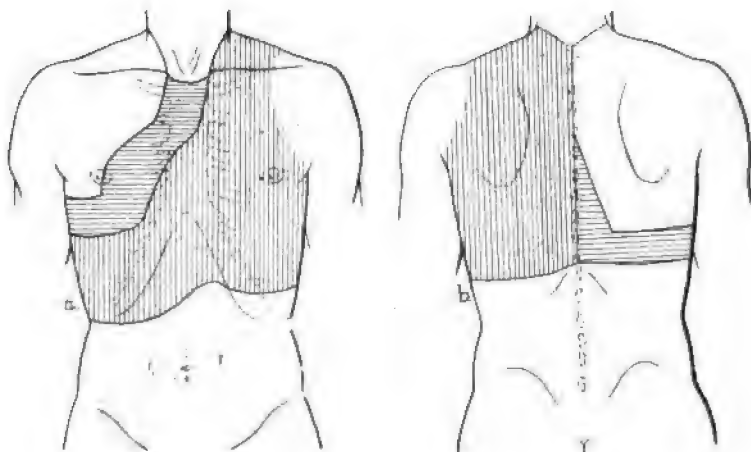
Fig. 184.—*a*, Anterior view; *b*, posterior view.   Large effusion.   Marked mediastinal and diaphrag-
matic displacement, seen posteriorly as "Grocco's sign."

dence of cardiac displacement may be quite inconstant.   In many
individuals the apex-beat may be lost.   This is particularly true

when the effusion occurs in the left side.   Right-sided effusions tend to produce evident signs of cardiac displacement.   The apex-
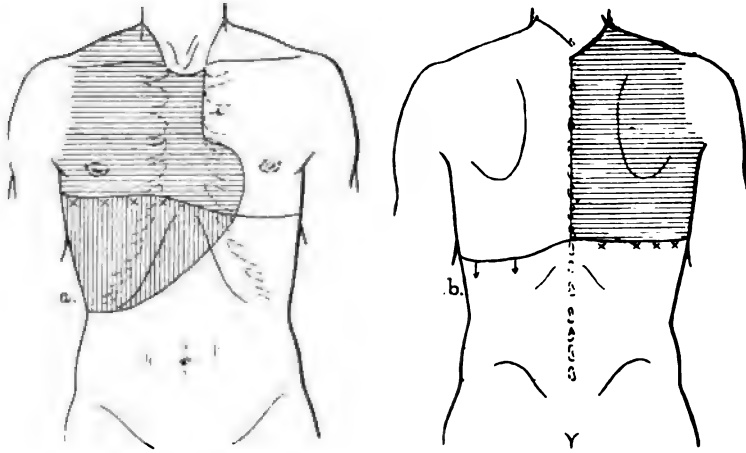
Fig. 185.—*a*, Anterior view; *b*, posterior view.   Retraction of apex and lower border of lung, with diffuse relative dullness, due to dense adhesions.
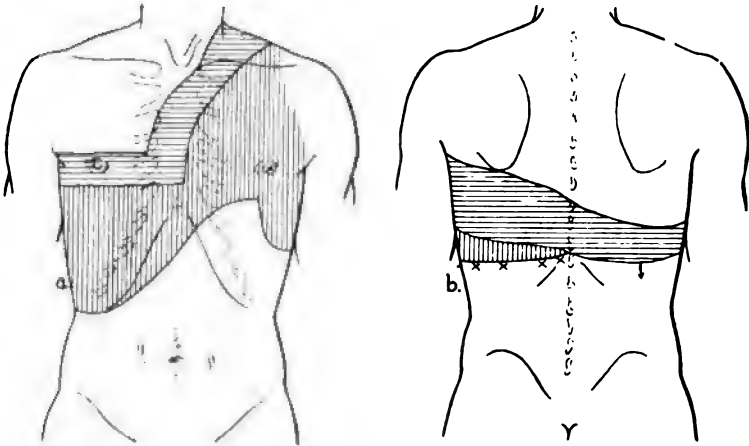
Fig. 186.—*a*, Anterior view; *b*, posterior view.   Outlines of a moderate effusion, altered by adhesions.   Effusion largely anterior.

beat is emphasized, if anything, and, as a rule, the cardiac dullness is extended beyond the left mammillary line.

Moderate effusions show a variable degree of encroachment upon Traube's space. If friction-rubs were audible at the outset,
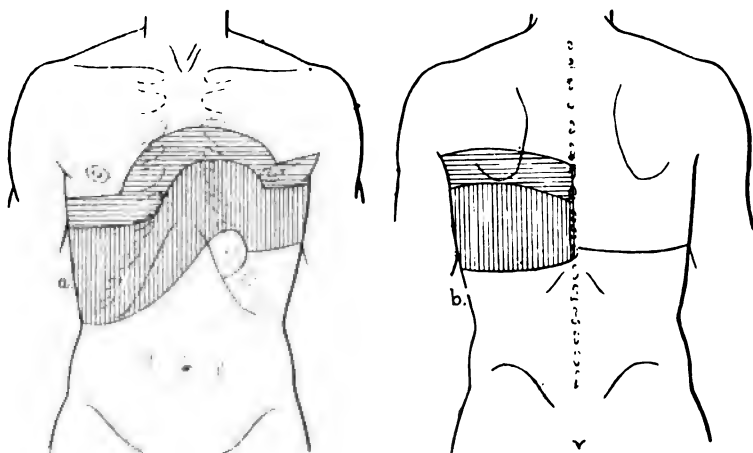
Fig. 187.—*a*, Anterior view; *b*, posterior view. Combination of pericardial and pleural effusion.
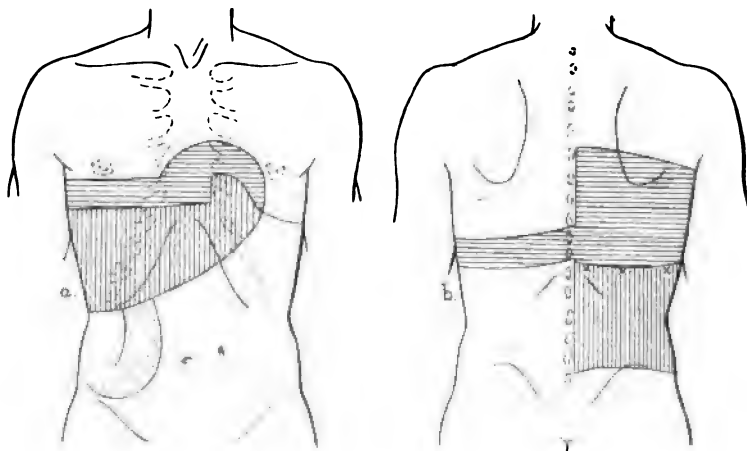
Fig. 188.—*a*, Anterior view; *b*, posterior view. Large paranephritic abscess. Right lung fixed at normal position by adhesions. Palpable mass below costal border.

their absence over the absolute dullness supports the diagnosis of effusion. As the fluid accumulates friction-rubs precede the rising

dullness.   This is particularly true anteriorly.   The breath-sounds on the affected side are markedly modified over the basal dullness, their intensity usually being much diminished.

The sound-producing qualities of the respiratory apparatus in different individuals vary so greatly that the measure of increased or diminished intensity must be considered relatively to corresponding areas on the unaffected side.   Basal breathing may be nearly or quite inaudible unless the patient increases the range and rate of the respiratory phase.   An intense vesicular breathing makes a
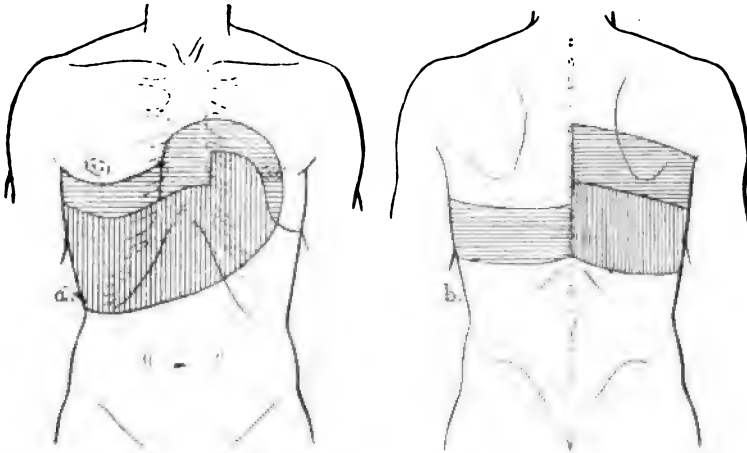
Fig. 189.—a, Anterior view; b, posterior view.   Case of mitral stenosis with pleural effusion due to infarct in right lung.

greater contrast in the breath-sounds over the exposed and the covered lung.   The relaxed lung at the upper border of the effusion offers favorable conditions for the increased transmission of the breath-sound.   This zone corresponds to the area of relative dullness, and over it a bronchial type of breathing is heard.   The usual relation of intensity of the breath-sounds suffers various modifications, depending upon the presence of other pathologic processes in the lung, pleura, or chest-wall, which affect the production or the transmission of respiratory sounds.

In large effusions the affected side is fully distended and quite
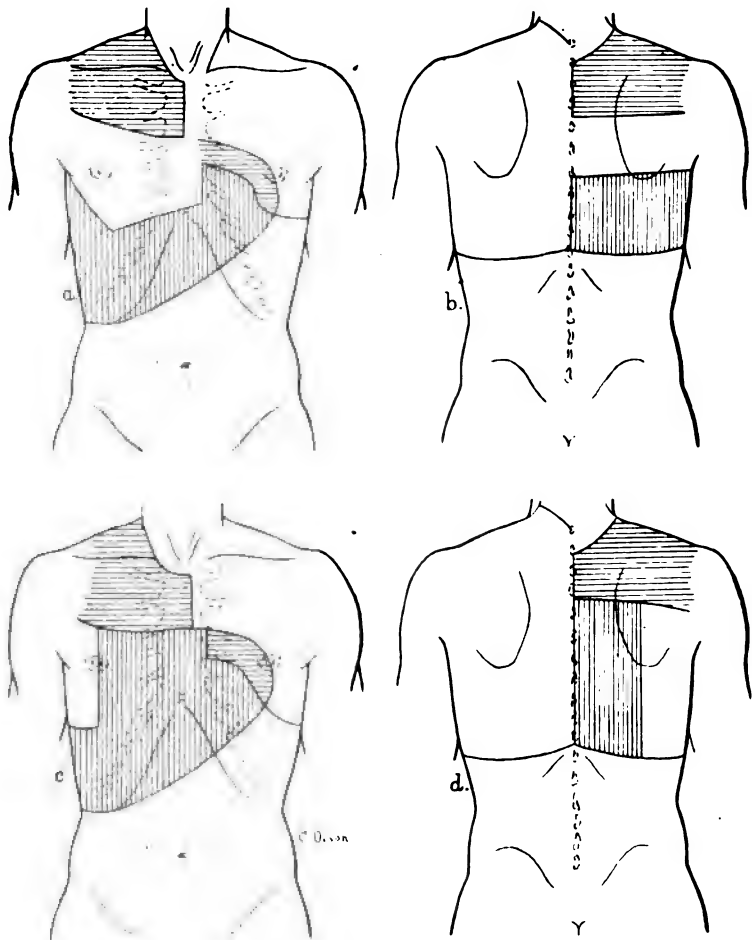
Fig. 190.—*a*, Anterior view, dorsal position. Mobility of fluid in the pleural cavity limited by adhesions over the upper portion; *b*, posterior view, sitting position; *c*, anterior view, right lateral position; *d*, posterior view, right lateral position. Pneumopyothorax in case of empyema with bronchial fistula.

↓   Normal excursion

×   Fixed lung border

▤   Relative dullness

▥   Absolute dullness
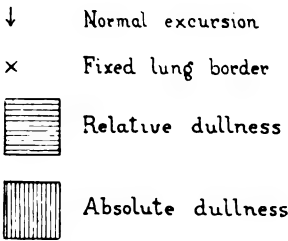
Fig. 191.—Key plate.

motionless. The asymmetry is greatest at the end of expiration. The interspaces are effaced, and the resistant feel of the ribs is markedly diminished when the hand is passed over the surface of the chest.

The percussion outlines are very characteristic. The relative dullness may be absent at the apex. In left-sided effusion the Traube space may be completely covered. The cardiac impulse may not be visible, or distinct pulsations may be seen at the right of the sternum or near the xiphoid. These unmistakable signs of the displacement of the mediastinum are very characteristic of large effusions. Posteriorly, the relative dullness at the base of the lung may extend considerably beyond the spinal column. Dyspnea and cyanosis are commonly presented. Usually marked diminution of intensity of the breath-sounds is observed, but at times one hears distinctly high-pitched tubular breathing.

The differentiation of massive pneumonia from large effusions is quite uncertain when the breath-sounds are relied upon too greatly. Either may be mistaken for the other.

In massive pneumonia fibrinous plugs may occlude the bronchi so completely that the breath-sounds may be absent throughout the affected lung, whereas in large effusions of the most pronounced types bronchial breathing may be heard.

Much dependence may be placed upon palpation, as it is quite infrequent for the palpatory sounds to be transmitted, while the audible ones may be transmitted in a marked degree. The most trustworthy findings are those of percussion, as evidenced by displacement of the mediastinum and diaphragm. With the recession of the fluid, either from absorption or from aspiration, the mediastinum assumes a more nearly central position. Often the friction-rubs are again audible or palpable.

The end-results of pleural effusions vary greatly, depending upon the extent and degree of the pleural inflammation. Much fibrinous or purulent inflammation results in the production of extensive adhesions. When repeated aspirations are necessary during the course of treatment, or in cases examined for the first time following a recent or remote pleurisy, it often requires careful

study to determine if fluid still remains or whether the physical
signs present are due entirely to resulting adhesions.   The range of
respiratory movement is much diminished, and the chest-wall
retracted, the affected side being the smaller.   All superficial evi-
dences of the descent of the diaphragm are lacking, and often one
sees instead fixed respiratory retraction of the interspaces.   The
fremitus is more or less diminished, dependent upon the degree of
pulmonary fibrosis.   A more or less intense relative dullness may
be present at the base or extend even to the apex.   If one can
determine accurately that the lung border is firmly fixed at approxi-
mately its normal level, fluid is quite certainly absent.   The inten-
sity of the breath-sounds varies directly in proportion to the degree
of retraction and fixation of the affected side.   At times a confusing
picture may be presented when, in addition to these signs, a local
bronchitis is added.

Having considered the physical findings which pleural effusions
present in general, it may be of interest to consider some of the
peculiarities of specific types of effusion.   In cardiac insufficiency,
or in chronic nephritis with retention of fluid, bilateral effusions are
met with which behave quite differently from the common types of
pleurisy.   Here cardiac displacement is uncommon.   Because of
the urgency of other symptoms, the presence of these effusions is
often overlooked.   They are frequently associated with hydro-
pericardium, ascites, and general edema.   At times posture, inter-
mittent infections of the pleura, or old pleural adhesions may act
as causes for the predominance of effusions in one side.

The most common cause of unilateral effusions in heart cases is
pulmonary infarcts.   The advent of such a condition is often
unheralded, although a classic onset, with pain in the side, increase
of dyspnea, and the spitting of blood, is the rule.   The development
of an effusion may be quite rapid and embarrassing, and demand
early aspiration.

In cases of partial obliteration of the pleura recurrence of
effusion may produce findings of curious types.   Usually these
adhesions are located at the base.   At times sacculated effusions
develop during the course of a single attack.   Such sacculations

may be multiple, and each may contain fluid of a different character. Interlobar empyema is a common type of such sacculation. Displacement of the mediastinum may occur, as in effusions involving the general pleural cavity.

Not infrequently cases appear for examination giving a history of pneumonia, followed by continued fever, during the course of which there has been sudden expectoration of a large quantity of pus. Such histories usually indicate either a lung abscess or an empyema. When the lung abscess is located at the base, the physical signs may be quite similar to those of empyema. The presence of elastic fibers in the sputum speaks strongly for lung abscess.

Cases of ruptured empyema give a picture similar to pneumo-pyothorax, with the exception of the symptoms caused by the fistula into the bronchus. The drainage is quite imperfect, and the expectoration of large amounts of purulent sputum occurs intermittently with paroxysms of coughing. Of course, much variation exists in the size and shape of the cavity occupied by the air and fluid, this variation being governed by the conditions established within the pleura by the empyema prior to the rupture.

At any time the signs evidenced depend upon the proportion of air and fluid occupying the cavity. The absolute dullness ends abruptly in the tympany directly over it, and its upper margin is always horizontal, irrespective of the position of the patient. It exhibits prompt mobility with each change in the position of the patient. Fremitus is absent over both the dullness and the tympany. Splashing is frequently heard by shaking the patient. Coin sounds are very distinctive when elicited. The breath-sounds are quite lacking in vesicular quality, and characteristic metallic overtones are imparted to both the râles and the splashing, and when the track of rupture is patent, a loud, whistling, fistulous murmur may be heard.

Pneumothorax may be considered with propriety in the consideration of pleural effusions. Frequently it complicates a tuberculosis with cavities. Its sudden onset, with pain and dyspnea, is very suggestive, especially when the patient is known to have

active tuberculosis.   Air furnishes the same possibility as fluid in producing physical signs, and according to the peculiar conditions at the point of entrance it may communicate freely with the bronchus or come intermittently; or, when a valve action occurs, it may acquire a positive pressure within the pleural cavity.

All degrees of displacement of the mediastinum and diaphragm may occur.   Air is even a poorer conductor of fremitus, voice, and breath-sounds than fluid.   The percussion findings are differential and characteristic, the whole side giving a loud tympanitic note with metallic overtones when the tension within is proper.   Coin sounds are also heard.   The condition is seldom overlooked when it is thought of.

Usually fluid appears early in such cases; in fact, it may so completely replace the air that only a small bubble may be found at the upper part of the chest.   When this is so, the recognition of the exact condition may not be possible unless one tests the mobility of the small area of resonance present.   If this small area shifts to the uppermost part of the pleural cavity when the patient is sitting, lying, or in a knee-chest position, the diagnosis of pneumohydrothorax is certain.·   By marking accurately the limitations of absolute dullness and resonance with a skin pencil, the outline and position of a small resonance at once become very suggestive.   The lines are invariably horizontal, and the mobility is seldom overlooked if the patient is percussed in the sitting and dorsal positions, as is usually done.   Prompt mobility of the dullness in cases of pleural effusion is found only where free air is also present in the pleural cavity.   In most cases of pleurisy with effusion, and especially in empyema, the dullness remains fixed. At times the dullness of hydrothorax may shift slowly—too slowly, in fact, to be noted during an ordinary examination.

In discussing the diagnosis of pleural effusion it is necessary to say a word about the use of the exploring syringe as an aid.   The physical signs furnish the data suggesting its use, and by its use the trustworthiness of these signs is tested.   In the great majority of cases where it is used the point of insertion of the needle falls within the area of absolute dullness.   Explorations within a relative dull-

ness usually yield a negative result.   Much is heard as to whether this or that point is the most suitable for a puncture.   Such rules presuppose a relatively large effusion occurring within a pleura which has suffered no complications from adhesions.

Effusion within the pleural cavities may occur as a complication or as an associated lesion in many different conditions.   Accumulation of pus beneath the diaphragm often furnishes findings easily confused with those produced by fluid within the pleural cavity.

It is scarcely within the scope of this paper to discuss the very great aid which may be rendered by the x-ray in the diagnosis of diseases of the chest.   It has been my aim to consider the subject from the standpoint of physical diagnosis, and not to include matters relating to the causes, symptoms, or morbid processes of these effusions.

VISCERAL PLEURECTOMY FOR CHRONIC EMPYEMA*

CHARLES H. MAYO AND EMIL H. BECKMAN

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Chronic empyema is a condition which is quite common in spite of the fact that it results, in most instances, from the failure of early diagnosis and the establishment of sufficient drainage in the acute stage. In the acute stage, if free drainage is established early and the adhesions are broken up at the time of the first drainage, the lung reëxpands quickly, thus obliterating the abscessed cavity, and the patient goes on to rapid recovery. In the neglected case in which the infected fluid remains in the pleural cavity for a considerable length of time the pleura becomes so thick and fibrous that even after free drainage is established the lung cannot reëxpand. In nearly all cases this is because of the adhesions and the thickened pleura, and not due to any extensive disease of the lung. It is true that in some cases there is an abscess in the lung which drains spontaneously into the pleural cavity, but this does not seem to be the usual way in which an empyema takes place.

In the chronic cases of empyema the ribs prevent the chest-wall from dropping in and the adhesions and the thickness of the pleura prevent the lung from reëxpanding. The result is a large cavity which continues to discharge varying amounts of pus. Nature cannot obliterate this cavity, as she ordinarily obliterates cavities by collapse of the tissues about it. Neither can she force granulations through the fibrous wall of the abscess.

Various methods have been devised by surgeons to obliterate this cavity. Estlander[1] resected the ribs subperiosteally over the

entire area.   The number of ribs resected varies with the size of
the cavity.   It is important to be radical and to resect one rib too
many rather than one too few in order that no dead space remains
in the upper or lower part of the cavity to continue suppuration.
Many surgeons have modified this operation; for example, Sau-
bouttin,[2] Beck,[3] Quénu,[4] and Tietze[5] resected small portions of the
ribs through parallel and vertical incisions of the region involved.
Jaboulay and Leymarie[6] divided the sternal attachment of the ribs,
making use of the articulation at the vertebral column to mobilize
the chest-wall, while Boiffin[7] recommends resection of the ribs close
to the vertebral column, making use, as it were, of the mobility of
the costal cartilages.   More recently, Wilms[8] has combined these
two operations and resects a couple of inches of several ribs along
the spine and also along the sternum in order to mobilize the chest-
wall.   Schede[9] noticed that some empyema cavities did not heal
even after extensive resections of ribs.   He observed that the thick-
ened pleuræ did not unite with each other, but directly impeded
recovery.   Consequently he devised the operation which bears
his name.   This consists of removing not only the ribs covering the
empyema cavity, but also the thickened parietal pleura and the
intercostal muscles, so that the skin and superficial muscles rest
directly against the thickened visceral pleura.   This operation is
usually performed through a U-shaped incision beginning along the
external margin of the pectoralis major muscle to the lower part of
the thorax and then backward and upward to the median line of
the scapula.   The skin, superficial muscles, and scapula are then
reflected upward, while the pleura, ribs, and deeper muscles are
removed over the entire cavity.   The operation is severe and the
shock to the patient is often alarming, if not fatal, especially since
many of these patients are in an extremely debilitated condition.

In 1893 Fowler,[10] operating on a woman thirty-five years of age
who had had an empyema with a fistula for ten years, dissected
out the scar tissue surrounding the fistulous tract and removed the
entire mass of fibrous tissue from the diaphragm and lung.   He was
surprised to discover that the lung began to reëxpand as soon as
this thick scar tissue was peeled from it.   The patient recovered

'14—30

from the operation and the wound entirely healed within a few weeks. The case was reported in December, 1893. In commenting on the case Fowler stated that the history suggested a method of dealing with some of the cases of old empyema with a persistent sinus which resist all the means usually employed for their cure.

Delorme,[11] after observing autopsy cases of old empyema, decided that the lung would reëxpand if the thickened pleura was removed from it. Consequently he devised the same operation and reported it about three months later—in the early part of 1894. Unfortunately, his patient died from hemorrhage and shock.

These two men performed the same operation and arrived at the same conclusions concerning these cases, the difference being that one of them performed the operation, following out the steps as he proceeded, while the other studied out the operation in advance and then performed it. Ransohoff,[12] following the work of Fowler and Delorme and appreciating the difficulty of removing the thickened pleura in some cases, advised making multiple incisions at right angles to each other, about ¼ inch apart, through the thickened pleura down to the lung, so that the entire visceral pleura should be gridironed. This is a valuable procedure and may often be used with good results in conjunction with visceral pleurectomy.

We believe that the operations of Fowler and Delorme have not received the attention from American surgeons which they deserve. We have been able to find but 24 cases reported in the literature by three operators in the twenty years that have elapsed since the reports of Fowler and Delorme. The efforts of surgeons up to the time of their reports had evidently been directed entirely to obliterating the cavity in chronic empyema by collapsing the chest-wall. They apparently had not appreciated the fact that in most instances the lung itself was not badly diseased and that it would reëxpand to a greater or less extent if given an opportunity. Even to-day the possibility of restoring a portion or even an entire lung to the patient is not fully appreciated. In this age of conservation it certainly seems worth while to attempt it even if we do not always succeed in restoring to the patient the use of a portion of such a valuable organ as the lung.

Keen[13] states that, as a rule, satisfactory results cannot be expected by this method if the operation is undertaken after four or five months have elapsed since the primary drainage.   Von Bergmann[14] tells us to try decortication of the lung when other methods fail.   If it is possible for.the lung to reëxpand in a reasonable proportion of the cases without involving more danger to the patient than by other methods, we accomplish everything that is accomplished by the other methods, and, in addition, restore to the individual the use of a lung or portion of a lung.   This factor certainly seems important enough to be considered seriously.   In previous years the results from the Estlander and Schede operations were so discouraging that, through a process of evolution, we have gradually taken up the operation of visceral pleurectomy in conjunction with these other procedures.

We wish to report two cases in which this thickened pleura was removed from an entire lung in an adult, in both cases more than six months after a primary drainage.

CASE I.—(A31028.)   Male, aged twenty years.   Date of operation November, 1911.   Patient had had typhoid fever.   Sick for three months following the typhoid, when an empyema was discovered on the right side and drained.   This was in January, 1908. It had been draining at intervals until he first came under observation.   Examination revealed a nearly collapsed lung on the right side, with an enormous cavity which extended from the diaphragm to the clavicle.   Through an opening large enough to explore the cavity the thick, fibrous pleura over the entire lung was removed. There were a number of fibrous bands which entered into the tissue or the lung and others that bound it to the diaphragm.   These were freed as well as possible.   The case was considered very unfavorable after the operation was finished.   To our surprise the lung soon filled the entire thoracic cavity, and drainage was entirely stopped by January 5, 1912, fifty-one days after the operation. There were good breath-sounds over the entire right thorax, the patient steadily gained in health and strength, and has remained entirely well to the present time.

CASE II.—(A77103.)   Male, aged twenty-three years.   Examined December 7, 1912.   The patient was shot with a rifle through the left chest in October, 1912.   The bullet entered from in front, passed entirely through the thorax, and was found lodged under

the skin of the back.   Three weeks later an empyema was drained.
When examined, the left thorax was shrunken, the patient was
very weak and emaciated, and the entire left lung was collapsed.
He was advised to return to his physician to get in better con-
dition to undergo a pleurectomy.

Fig. 192.—Before operation.

Six months following the primary drainage, in May, 1913, he
returned for operation.   A complete visceral pleurectomy of the
left lung was made.   The thickened pleura was removed from the
lung, diaphragm, and pericardium as well as possible.   There was
very little bleeding, and, although the patient was emaciated and
weak, there was almost no shock following the operation.   Drain-

age ceased entirely in three months.   There were good breath-
sounds over the entire thorax, and he had gained 19 pounds in
weight.   Two months later he returned with a small collection of
pus in the pleural cavity under the left axilla.   This was drained.
The patient still has a small cavity at this point which will require

Fig. 193a.—Before operation.

further operation, but at least two-thirds of the lung is function-
ating.

These two cases illustrate the possibility of a collapsed lung
reëxpanding, even after many months.   We do not intend to say
that such results can be accomplished in every case of chronic
empyema, and we realize that pleurectomy must be combined with

resections of ribs and the Ransohoff technic in most instances.   We
wish to emphasize the fact that in our experience pleurectomy has
not produced anywhere near the same degree of shock that the
Schede operation does.   We believe that in most instances it should

Fig. 193b.—Some weeks after operation, showing reëxpansion of major part of the lung.

be attempted before extensive resections of ribs are undertaken.
If the lung only partially expands, resections can be done at a
second operation without any loss except the time of the patient.

Tuffier[15] recommends that with the patient in poor condition

the operation be divided into several stages, rather than attempting to complete it in one stage. He also recommends the Delorme operation in selected cases. We also believe that many of these cases should be operated on in stages, and pleurectomy can be attempted. If this does not obliterate the entire cavity, one usually gains some lung expansion and the remainder of the cavity can be obliterated later by the Estlander or Schede operation.

We wish to report two other cases in which the wound healed primarily following pleurectomy.

CASE III.—(A71074.) Male, aged twenty-two years. Patient with a left-sided empyema following pneumonia, which had drained at intervals for thirteen months. A cavity six inches in diameter posterior to the pericardium was explored, and the thick membrane covering the pleura and diaphragm removed. The cavity healed entirely in thirty-nine days.

CASE IV.—(A73419.) Male, aged eighteen years. Patient had a left-sided empyema which had drained for over two years. At operation a cavity the size of a large grape-fruit was found external to the pericardium. The thick membrane was peeled from the lung and partly from the pericardium. The cavity closed in three weeks.

In discussing the treatment of such cases a word should be said in regard to the preparation of the patients for operation. Many of these patients are as much in need of preoperative preparatory treatment as patients about to undergo an operation for prostatectomy.

It is very important that the drainage should be at the most dependent part of the cavity. We have seen several patients gain from 15 to 25 pounds in a few weeks with a corresponding gain in strength by changing the point of drainage to the most dependent part of the cavity. Autogenous vaccines should also be employed. After the patient has stopped gaining, following such an operation for drainage, and is in the best condition possible, irrigation of the cavity twice daily with a weak iodin solution helps reduce the infection to a minimum. In regard to the operation itself, sufficient exposure must be obtained to make every portion of the cavity

freely accessible. The entire cavity should be cleansed as thoroughly as possible, and then swabbed with strong tincture of iodin before pleurectomy is begun. The incision through the thickened pleura is best started posteriorly along the vertebræ, as there is less danger, especially on the left side, of entering the pericardium. One need not fear slitting entirely through the thick pleura down to the healthy lung, as the bleeding does not seem to be excessive, and, although the lung has been injured enough to allow air-bubbles to escape, in almost every instance no harm has arisen from such injury, and apparently no extensive infection to the lung by such exposure has occurred. Pneumonia did not occur in any of our seven cases in which pleurectomy was performed. Abundant drainage to the furthest points of the cavity should be provided for by small gutta-percha drains to prevent re-accumulation of the fluid in the pleura. One operative death has occurred. With our present knowledge we believe that too extensive an operation was attempted on this case. Now we divide the operation into stages when necessary.

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RECOVERY FROM PARALYSIS FOLLOWING DECOMPRESSION OF THE SPINAL CORD*

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Surgery of the central nervous system is coming to be recognized as a branch of surgery in which the results may be compared favorably with those secured in many of the other special lines of surgery. Much of the haze of uncertainty which surrounded the diagnosis and treatment of diseases of the central nervous system has been cleared away by the brilliant light shed upon it by such investigators as Horsley, Sherrington, Cushing, Frazier, Spiller, Mills, *et al*. Investigation and experimentation have led surgeons of ability to attempt to cure by surgical means many lesions of the central nervous system formerly considered hopeless.

As a general rule, laparotomies and operations on the extremities that fail to reveal the pathologic lesion diagnosed or which disclose a neoplasm which cannot be removed are likely to be considered as failures. Yet all surgeons are familiar with many instances of relief from symptoms and retardation of the growth of malignant abdominal conditions following an exploratory laparotomy. The rapid cure in tuberculous peritonitis that sometimes follows an exploratory laparotomy is an illustration. In performing operations on the brain the same relief of symptoms and an occasional cure when no pathologic lesion is demonstrated is so common that the operation known as decompression is perhaps the commonest one performed on that organ. In this instance, however, the relief is believed to be due to the removal of pressure, yet in most instances no cerebral hernia develops and the escape of

cerebrospinal fluid must be of short duration. Is it not reasonable to suppose that the same factors that produce the improvement following an exploratory laparotomy may also assist here?

While the operation of decompression in brain surgery has become a recognized procedure, its application to the surgery of the spinal cord is more recent. The relief of symptoms following decompression of the spinal cord is at times as wonderful, and the beneficial results obtained as surprising, as that obtained in cerebral decompression. When a diagnosis of tumor of the spinal cord has been made on a patient with root pains, level symptoms, disturbed sensation, and paralysis, and the operation fails to reveal the supposed tumor, it is truly humiliating to the surgeon; but if after such an experience the pain disappears, the paralysis leaves and the sensation returns, the result is almost as gratifying to the surgeon as to the patient.

I wish to present two cases—one with no demonstrable lesion, the other with possible tumor—to illustrate the beneficial results that sometimes follow spinal decompression:

CASE I.—(A67505.) Male, married, aged forty-nine. Occupation, merchant. Examined May 6, 1912. Previous history negative. Patient had suffered for several years with indefinite pain about the waist and down the thighs and legs. Occasionally the pain was severe for several days. He was operated on for appendicitis six years ago, during a periodic attack of pain which was believed to be appendicitis. He has had the same attacks many times since. One year ago weakness in the right leg was noticed, which disappeared in two or three weeks. Six months ago gradual weakness appeared in the left leg. Five months ago there was some swelling in both legs. Three months ago the left leg became so weak a cane was used in walking, and for the past two months, because of the weakness in both legs, he has been unable to stand. He is now confined to a chair and cannot move his legs about voluntarily. He suffers continuous pain in the lumbar region which radiates around the body and down the thighs; there is involuntary contraction of the muscles of the thighs and legs associated with pain when the legs stiffen. Some difficulty is noted in starting urine, but no actual loss of bladder control.

There is disturbed sensation below the level of the second lum-

bar vertebra, and heat and cold are not recognized below this level. The knee-jerks are much exaggerated. Ankle-clonus and Babinski's sign are present. The Wassermann reaction of blood and spinal fluid are both negative. Diagnosis—tumor of the spinal cord.

On May 16, 1912, laminectomy was performed, and the arches of the fifth, sixth, seventh, and eighth dorsal vertebræ were removed. The dura was opened, but no lesion found. The diagnosis of tumor seemed so positive that on May 24th the arches of the tenth, eleventh, and twelfth dorsal vertebræ were removed, but no lesion was discovered except a small lipoma lying on the dura. This apparently caused some pressure, but could not account for the paralysis. The cord appeared normal, though congested. The wounds healed primarily. The patient suffered severely for several weeks from the spastic condition of the legs, which was associated with severe pain. At the present time, two years and seven months since operation, he is absolutely free from pain, has regained normal strength in the thighs and legs, and is able to perform all movements. He gets about on his hands and knees and rides horseback. We have not been able to examine this patient, but from reports the only reason he is not able to walk is on account of the contractions which took place while he was suffering from the spastic condition. Undoubtedly these contractions could be relieved by orthopedic measures and he would be in a normal condition.

CASE II.—(A 102880.) Single, male, aged thirty. Occupation, a wood worker. Examined March 23, 1914. Seventeen years previously, while playing foot-ball, the patient injured his back and was unconscious for about two hours and had partial loss of power in both legs for two weeks, so that he was unable to walk. The bladder and bowels were not involved. He entirely recovered and was able to play foot-ball in a month. One year later he noticed a slight drag in his left leg, which seemed to be a loss of power in the muscles without any disturbed sensation. An orthopedist told him that the second lumbar vertebra was dislocated. At this time there was severe pain of a lancinating character which extended down the spine from the lumbar region and into both sciatics. Three years later, in 1901, there was still some loss of power in the left foot, and he also had sudden severe pain in the back under the scapulæ, which seemed to produce a spasm of the muscles of the back. He had a temperature of 101° for three days, was in the hospital for six weeks, and part of the time morphin was required to control the pain. After that he was in his usual health until four

years ago, when his left leg became weaker, and he had pain in the left hip and knee. From this time on he has continued about the same, with pain in both the left and right thighs, knees, and legs, with gradual loss of power of both legs. The bladder control is weak but not entirely lost. In December, 1913, the patient had sudden severe pain between the shoulders and the back of the head, which caused a retraction of the head. The diagnosis at that time was meningitis. The patient thinks he had some increase of temperature, but was in his usual health in two weeks.

Physical Examination.—Patient is small and thin. General examination was negative, with the exception of possibly a slight deformity at the first and second lumbar vertebræ. He is not able to walk, and is unable to lift either foot from the floor, although the feet and toes can be moved. The knee-jerks are exaggerated, and he has marked ankle-clonus. The spine seems rigid in the upper lumbar region. Tactile sensation, as well as the sense of heat and cold, is markedly impaired below the level of the second lumbar vertebra. The sensation is almost if not completely lost in the left thigh and leg, but not so much impaired on the right. The spinal fluid is negative, and Wassermann reaction from the spinal fluid negative.

On April 13, 1914, a laminectomy was performed and the arches of the ninth, tenth, and eleventh dorsal vertebræ removed. The dura was tense, but not bulging. On opening the dura the entire canal was found filled with dilated blood-vessels which resembled an angioma. One of these vessels was accidentally punctured in opening the dura, and the hemorrhage was severe. In order to control this hemorrhage it was necessary to pack the opening in the dura with a strip of gauze. The bleeding was easily controlled in this way. The dura was not stitched, but the muscles, fascia, and skin were closed with catgut. The gauze pack was removed on the fourth day and the wound healed primarily. The patient remained under observation until May 20th—thirty-seven days. Examination at this time showed that sensation was the same as before the operation. The bladder control has been almost perfect since the operation. There has been marked improvement in the motion of both legs; the patient can flex and extend the knees, can stand alone and walk several steps without support. The spasticity has also improved.

On June 20th, sixty-seven days after operation, the patient wrote as follows: "I have not had any pain since I returned. I am improving nicely so far as gaining strength is concerned, as I am

.now able to go around without my crutches considerable, and think I will be able to do away with them entirely in a short time. I have some twitching in my left leg, especially at night." On September 27th, five and one-half months after the operation, the patient wrote: "I am doing nicely so far and have been able to return to my work at last. I have not had a single pain of any kind except a burning sensation in my left thigh, which starts just above the knee and spreads over the front. There is also some slight twitching in my legs. This is only occasionally, and may be absent for several days at a time."

It is impossible to say whether these patients are cured or only temporarily improved, but the results have already justified the operation.

SOME OBSERVATIONS ON THE OPERATIVE TREATMENT OF TUBERCULOSIS OF THE SPINE*

MELVIN S. HENDERSON

Tuberculosis of the spine is a disease relatively common, and is accompanied by a high mortality. Generally speaking, as observed in orthopedic hospitals for children, tuberculosis of the spine is almost as common as tuberculosis in all the rest of the joints in the body. All things considered, a weakening of this bony column by tuberculosis is more far-reaching in its results than tuberculosis elsewhere in the body. Complete paraplegia may, and too often does, follow. The treatment of tuberculosis of the joints is gradually being placed upon a sound surgical basis. The pendulum has swung from extreme radicalism to almost extreme conservatism, but is gradually assuming its proper position. For many reasons it is best to treat tuberculosis of the joints in children conservatively, whereas the opposite is true, in a certain percentage, of tuberculosis of joints.in adults. So many conditions determine the line of treatment that there will always be a difference of opinion among surgeons as to the course to pursue. In no other branch of surgery is the saying so true that each case is a law unto itself as in the treatment of tuberculosis of the joints. Definite lines of treatment may be laid down for cases treated in large charitable institutions for indefinite lengths of time, but these fixed rules cannot be adhered to in the private clinic.

Tuberculosis of the spine usually involves one or more of the

vertebræ.   In tuberculosis of the knee in adults we know that by removing the bulk of the diseased tissue we attain an ankylosis and a cure of the disease.   We cannot, for anatomic reasons, re-move the diseased tissue in the spine.   Cases must be treated by fixation with apparatus and an ankylosis of the diseased joints awaited to bring about a gradual subsidence of the disease.   Rarely, though more often in children than in adults, we may obtain a cure without any destruction.

About three years ago the idea was advanced by Hibbs[1] to hasten this process by operative procedure. .He advised a plastic operation on the spinous processes and the laminæ of the diseased vertebræ, which are practically always free from disease, to form a strong posterior splint by ankylosing the posterior portions of the vertebræ (Fig. 194).   That an ankylosis is thus secured he has since shown by specimens obtained at postmortem.   Almost at the same time Albee[2] suggested obtaining a like result by grafting a piece of bone obtained from the tibia of the patient to the spinous processes over the diseased area (Fig. 195).   Albee has shown, by specimens, that the bone-graft becomes firmly attached to the spinous processes and provides fixation.   It should be recognized that these operations are not so radical as that of excising tuber-culous knees or shoulders, and are merely means of providing fixa-tion.   Rapid cures should not be expected, as may be looked for following excisions.   Previous to the introduction of these opera-tions fixations were obtained by the aid of plaster-of-Paris jackets and braces, and they were good aids.   By means of the bone-graft, or the plastic operation, however, we hope to provide a bony splint which will be permanent and more efficient than the jackets and braces.   These operations promise to be a great aid in the treat-ment of tuberculosis of the spine, but for the reason stated above we must not expect too rapid a cure (Figs. 196 and 197).

From August 1, 1912, to July 31, 1914, 39 cases of tuberculosis of the spine had been operated on in the Mayo Clinic—33 cases were done by the Albee method and 6 by the Hibbs method.   I should like very much to report all these cases cured, but after carefully tracing all but one and personally examining the major-

ity of them, I cannot do so. I may say, however, that these patients have, on the whole, done very well; I consider the operations of great value in the treatment of the disease, but they should

The Hibbs' Operation. Fig.1
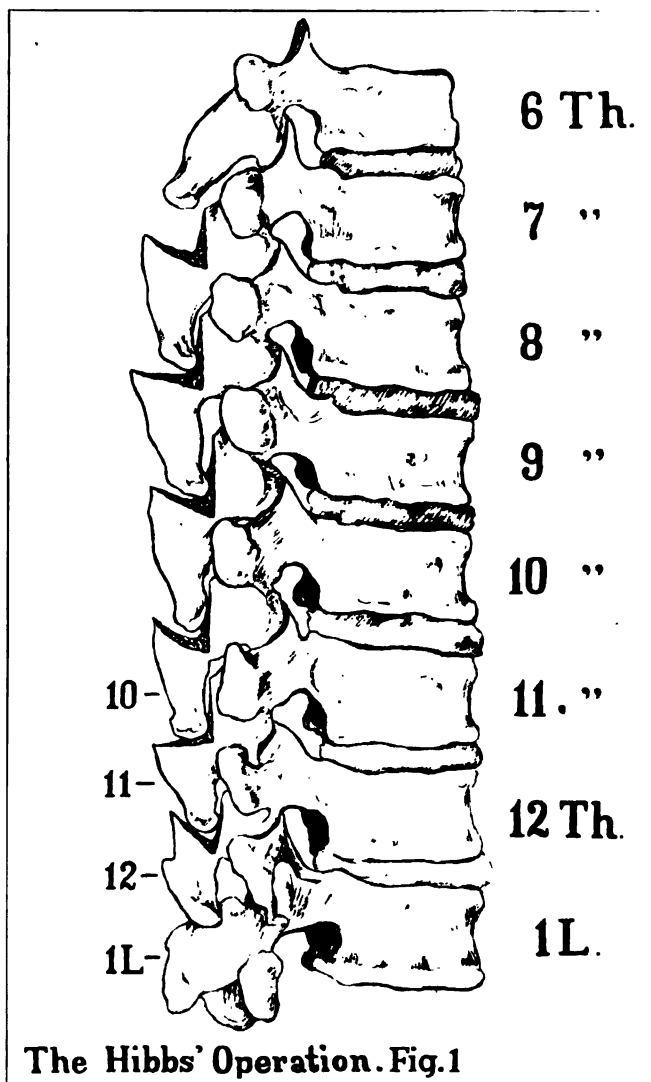
Fig. 194.—The Hibbs' operation.

be considered only an aid and not the sole treatment.   All the
patients in our series have been requested to wear the brace for
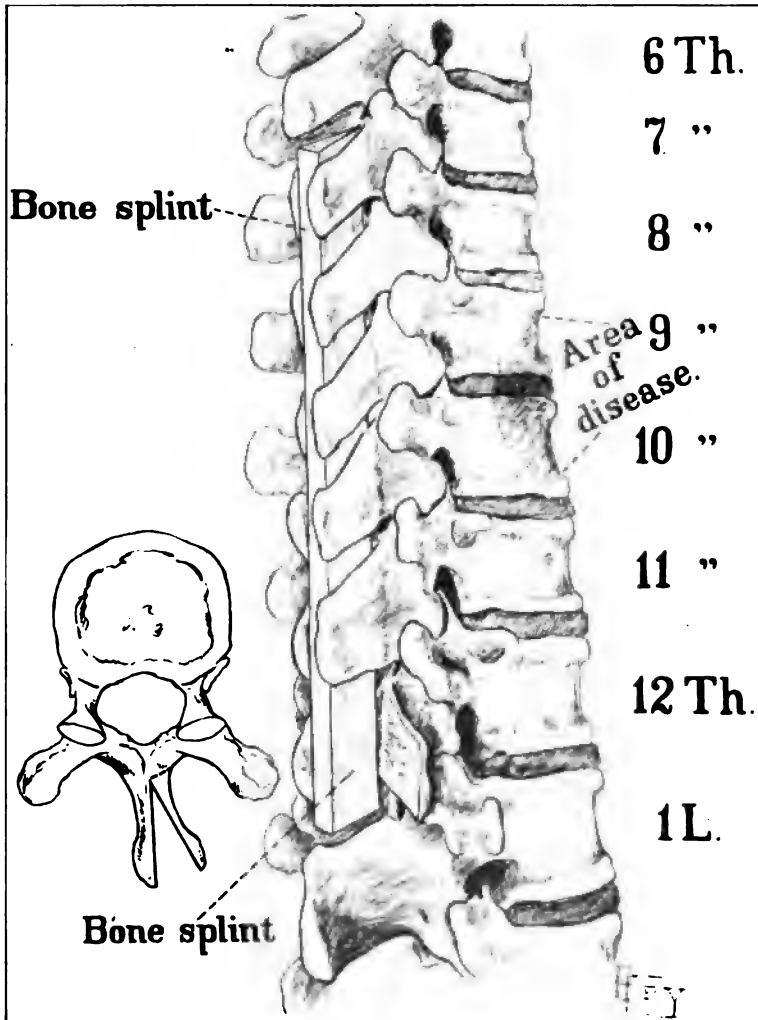
Fig. 195.—The Albee operation.

at least one year after the operation, and preferably one year after
the cessation of all symptoms, observing, of course, all the ordinary

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hygienic treatment usually given tuberculous patients. To my knowledge only two are going without their braces—one I consider cured, the other very much improved. The majority of those examined one year or more after operation do not show absolute fixation on flexion of the spine. Clinically, these cases show a lack of muscular spasm and are nearly well. I believe, however, that there is a sufficiently large area ankylosed to fix the diseased joint, and that the motion we see occurs at the ends of the inserted graft. This emphasizes the point that the graft must be long enough to extend beyond the diseased area, above and below, for two vertebræ.

The operation in the adult is not attended by any reaction, but little children two and three years of age show the effects and the operation should not be unnecessarily prolonged. There has been no operative mortality in our series. Recumbency on a stiff bed has been insisted on from four to five weeks in adults and two to six months in children. In all cases a modified Taylor brace has been provided for use in getting about. There are but five children in our series, ages from two to seven years. An x-ray of the youngest showed no evidence of the graft one year after operation. I cannot explain this except to say that operative bone work in children does not seem to follow the same course as in adults. Clinically, this child is very little better than he was before the operation. In the x-ray of the adults the grafts show clearly one year and more after operation. The case of longest standing is only two years. Sufficient time has hardly elapsed to enable us definitely to say whether or not the cases are cured. The fact that my deductions seem somewhat indefinite may be explained by the nature and location of the disease and our failure to eradicate it. Of the 39 cases, 27 were males and 12 females; age of youngest two, age of eldest, fifty-three; average age, twenty-seven years. The average duration of symptoms before operation was three and one-third years. There seemed to be a definite etiologic factor in 11 cases. By this I mean that some member of the family had tuberculosis, the patient had been closely associated with a tuberculous patient, or previously had had a

tuberculous focus himself. It was proved that 7 patients had tuberculosis of the lungs, but only 1 was active at the time of operation. In 4 cases trauma seemed to have a definite bearing on the onset. Under this heading I included 1 patient unaccustomed to manual labor who had performed an unusual amount of work which seemed to mark the beginning of the trouble. The question of trauma associated with tuberculosis has recently been reopened by DaCosta,[3] who believes it to be the indirect cause of the lesion in a certain definite number of cases.

In 16 of our cases the lesion areas were located in the lumbar region; there were 8 in the lower dorsal, 7 in the dorsolumbar, 7 in the middorsal, and 1 in the high dorsal. Nine cases in the series had had previously or at the time of operation tuberculous foci elsewhere than in the lungs.

The degree of disability of patients operated on has been arbitrarily classified on a basis of 4: 1 signifies inability to work, but able to walk fairly well; 2 signifies the same except that the patient tires more easily and leans on objects as much as possible to relieve the weight on the spine; 3, patients in wheel-chairs; and 4, are bedridden.

Seven cases are classified under Group 1. Of these, 1 is too recent to report; 1 has not been traced; 1 may be called cured; 1 is improved and 3 are much improved.

Of the 14 classified under Group 2, 5 are too recent to report, one died later of acute pulmonary tuberculosis but was cured of his tuberculosis of the spine; 4 are reported merely as improved, and 4 are much improved.

There are 13 in Group 3. Of these, 2 are too recent to report, 5 are improved, and 6 are much improved.

In Group 4 there were 5 bedridden patients, and of these, 1 is too recent to report; 1 died; 1 is no better; and 2 are improved. The patient in this group who died had tuberculosis of the fifth lumbar vertebra. She had a marked double psoas contraction, a bad prognostic sign. Pain was severe and, thinking we might relieve this by fixation, an Albee operation was performed. The operative recovery was uneventful, but the pain was not relieved,

and she died some two months later.   No autopsy was obtained by
her physician.   Her abdomen was said to be full of pus—probably
a tuberculous peritonitis.   This case emphasizes the point that
the operation should not be performed on patients *in extremis*.

A careful unprejudiced review of this series of cases shows that
1 is no better, 9 are too recent to be reported, 1 has not been traced,

Fig. 196.—(106308.)   Tuberculosis of the spine in the lower dorsal region.   Note the abscess forma-
tion just posterior to the cardiac shadow

2 were cured, but 1 of these died later of acute pulmonary tuber-
culosis; 12 were distinctly improved, and 13 were much improved.
One died later of the disease.   Operation was recommended only
in those cases showing bony destruction in the radiograph.

Details of the technic will not be given in this paper.   A motor-

propelled saw is of considerable aid in removing the bone in the
Albee type of operation. One may work with it more quickly

Fig. 197.—(106308.) Showing the bone graft in position.

than the chisel, and is less apt to fracture the tibia, and the graft
is more easily obtained from the flat internal surface of the tibia.
In most of our cases we used a curved elliptic incision for the wound

in the back, but have abandoned this because in two cases an area of necrosis occurred at the edge of the flap, with disastrous results in one case, since the discharge from a sinus near by caused an infection of the wound. The graft will probably have to be removed. In the other case in which this occurred healing by granulation took place and the graft healed in.

Our first cases after operation were placed on a Bradford gaspipe frame, but now we merely stiffen the bed by placing a door between the mattress and the springs and insist on recumbency for one month. The brace is provided before the patients are allowed to sit up.

The Hibbs type of operation has the advantage that only one incision is necessary, and is often the operation of choice where the kyphos is very marked, but in a case with not too much deformity the Albee operation permits more rapidity of technic.

In conclusion I may say that these operations definitely shorten the treatment of tuberculosis of the spine; that they give a means of hastening the curative ankylosis so necessary in this disease, but that they should not be allowed to supplant recognized orthopedic appliances. Many patients are unable to visit or to be under the care of an orthopedic surgeon long enough to carry out the treatment satisfactorily by plaster-of-Paris jackets or braces. It is in these cases that operations will greatly help the surgeon to attain his object, i. e., of procuring an ankylosis of the diseased area.

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BIFURCATION OF THE TRANSVERSE PROCESS
OF THE FIFTH LUMBAR VERTEBRA*

MELVIN S. HENDERSON

Considering the length of the spine and the number of bones entering into its composition, it is not strange that abnormalities should be comparatively common. When we consider that the spine is composed of three or rather four distinct types of vertebræ, it is only natural to suppose that any abnormalities in these bodies would occur in the region in which there is a change from one type to another. Cervical ribs are most often found on the last cervical vertebra, that is, the last cervical is taking on the characteristics of the first dorsal vertebra. In the dorsolumbar region, also, we meet with abnormalities. The last dorsal may take on the characteristics of the first lumbar, giving us 11 dorsal and 6 lumbar vertebræ, or the first lumbar may take on dorsal characteristics, giving us 13 dorsal and 4 lumbar vertebræ. Again, in the lumbosacral region there is a transition from one form to another. The sacral vertebræ, originally 5 in number, become one to articulate with the ilia at the sacro-iliac synchondrosis. The change from the lumbar type to the sacral type is here made by a widening and flaring of the transverse processes, which coalesce to form the large ala of the sacrum.

The normal number of vertebræ may be said to be 26; the sacrum and coccyx counting as one each, and the twenty-fifth vertebra as the sacrum. However, as has been stated, the number of vertebræ may be diminished or increased by one. If diminished,

the twenty-fourth would be the sacrum as in the orang-utan and, if increased, the twenty-sixth would be the sacrum.

Rosenberg,[1] in his studies of the fetus, states that the first sacral is the twenty-sixth vertebra, but in the process of development the hip bones move upward, incorporating the twenty-fifth to form the sacrum. The development may go further and include the twenty-fourth, or it may be only partial, forming the so-called lumbosacral vertebra, joined on one side to the sacrum, but on the other having a normal or nearly normal free transverse process.

The ordinarily so-called lumbar ribs are not uncommon, but are practically never of any clinical significance. For this reason they are not usually found except by the Röntgen ray, either in the examination of renal lesions or in bismuth intestinal examinations.

A review of the abnormalities of the accessories of the vertebral bodies shows that it is indeed only the rare cases that cause symptoms, and they are relegated more to anatomic curiosities than to definite clinical entities. That they do occasionally cause definite symptoms there is no doubt, and we should familiarize ourselves with the conditions. Under certain circumstances great degrees of deformity may be present with very few symptoms. I have seen two cases in which the fifth lumbar vertebra was pushed down on to the anterior surface of the sacrum, so that the superior surface became anterior, and the anterior the inferior, surface. In both cases there were but few symptoms, the patients walking about doing their daily work. Marked lordosis was, of course, present.

The transverse process of the fifth lumbar vertebra quite often is abnormal in that it is broader, and in the radiograph appears to bifurcate (Fig. 198). In looking into the development of the transverse process of the lumbar vertebra it seems to be the consensus of opinion that it is analogous to the costal processes in the dorsal region. Woolsey[2] says that the transverse lumbar processes are in reality costal processes. Holl[3] claims that the transverse processes of the lumbar vertebræ do not represent ribs, but Bardeen[4] says the transverse process of the adult lumbar vertebra rep-

resents in the main an ossification of a membranous, non-cartila-
ginous extension of the fused costal element.

The transverse processes of the lumbar vertebræ are a com-
pound of a transverse and costal element. Some good-sized
foramina are usually to be located and represent the costo-trans-

Fig. 198.—(24159.) Bifurcation on the left side. Normal on the right. Probably articulating with the ilium. Mild sciatica right side for eight months, probably caused by tilting of the fifth lumbar Operation is not advised

verse foramina between the accessory or true transverse process
and the costal element.[5] The ala of the sacrum is in reality the
costal process, though so greatly changed as to be scarcely recogniz-
able (Fig. 199).

In view of these facts it would seem that the bifurcation of the

transverse process of the fifth lumbar vertebra is in reality an
overdevelopment of the costal element.   It could scarcely be called
a lumbar rib, and is probably the fifth lumbar vertebra taking on
some of the characteristics of the sacral vertebra.   The widened
process imitates the ala (Fig. 200).

These anatomic abnormalities of the fifth lumbar have been
recognized for some time, but it was not until Goldthwait called
attention to the possibilities of abnormalities of the articular
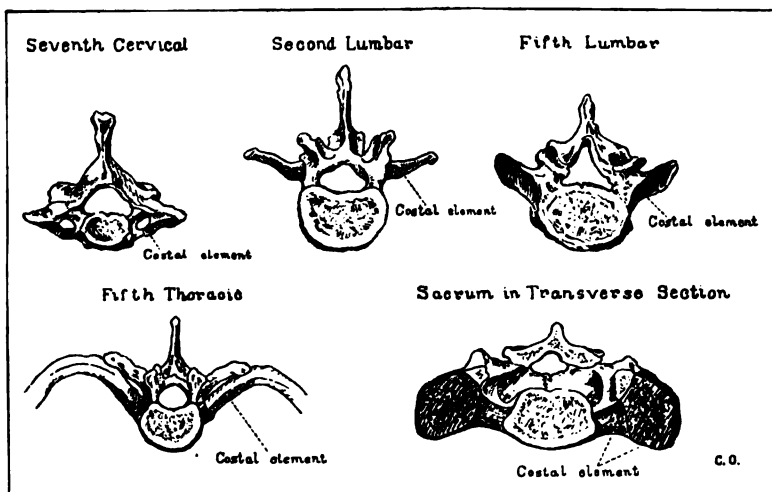
Fig. 199.—Costal element traced in various vertebræ.

and transverse processes causing serious symptoms that they were
considered anything but anatomic curiosities.

It is not my purpose to discuss in this paper the conditions
which might arise from the leverage action of these prolonged
and bifurcated transverse processes, but merely to point out that
the bifurcation of the transverse process of the last lumbar verte-
bra is relatively common and probably rarely causes symptoms.

In accounting for the symptomatology, or lack of it, in these
cases many things should be considered.   Goldthwait[6] called
attention to the variation in the width of the sacral bone and

the marked variation in the length and breadth of the transverse processes. This is only one of the several factors which may cause a dislocation of the fifth lumbar vertebra, bringing on a paralysis. Paraplegia occurred in one of Goldthwait's cases, and, in an attempt to explain it, his study was undertaken. He
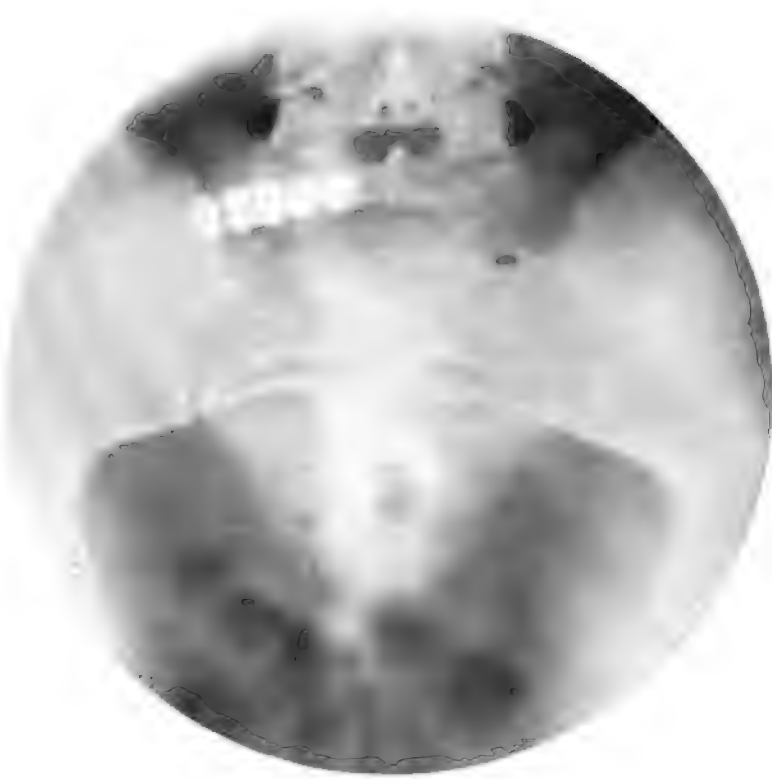
Fig. 200.—(96525.) Marked double bifurcation o the transverse processes of the fifth lumbar, illustrating how they may coalesce with the ala of the sacrum. Impossible to determine whether there is merely an articulation or whether the fifth lumbar has become a part of the sacrum. No symptoms.

stated briefly that if the transverse processes of the fifth lumbar vertebra were long enough to impinge on the iliac crests or top of the sacrum, certain side movements, if forcible enough, might act as a lever, tilting and twisting the fifth lumbar on the sacrum and causing pressure on the lumbosacral cord.

In the series of cases with enlarged or bifurcated transverse processes of the fifth lumbar which I am reviewing no such serious results were found. Symptoms were commonly absent, and in this were analogous to the cases with cervical ribs. Given a patient with long fifth lumbar transverse processes and a narrow-

Fig. 201.—(18202.) Bifurcation on the right. Normal on the left. This patient was operated on. The part of the process impinging on the sacrum and ilium was removed, with only temporary relief of symptoms.

based sacrum, pain is likely to be present. A patient with long bifurcated transverse processes and a broad-based sacrum would probably not have symptoms. The type of the individual must be considered in these cases, since many of the symptoms may occur in the so-called neurasthenic patients.

The operation of removing the process is a difficult one, due to the depth of the transverse process, and usually the operator is satisfied with the removal of only a part of the process.

Within the last two years 17 cases with bifurcation of the transverse process of the fifth lumbar vertebra have been recorded in our clinic.   In this series there were 3 males, aged from eighteen

Fig. 202.—Posture caused by the elongation of transverse process of fifth lumbar vertebra on the left side.

to thirty-five, and 14 females, aged from nine to forty-five years. Only 3 gave any symptoms which could be definitely attributed to the condition present.   The remaining 14 cases were discovered accidentally in radiographing for other conditions, such as lesions of the kidney and ureter, tuberculosis of the spine, congenital dislocation of the hip, etc.   In 4 cases the condition occurred on both

sides, 7 on the right, and 6 on the left.   One case only was operated on; relief was but temporary.

CASE 1.—(95236.) F. K., female, aged twenty-five years, married. Patient complained of steady backache across sacro-iliac area for eight years.   More severe on leaning over.   Worse since childbirth.   Some steady pains in calves of the legs.   Sleeps well.   On account of the steady character of the pain and well-marked bifurcation of the right transverse process of the fifth lumbar, operation was advised, but deferred by the patient.

CASE II.—(90328.) E. V. O., female, aged twenty years.   For eight months had complained of pain in right hip, gradually growing worse, and extending down the leg to the back of the right calf.   Considerable loss of sleep.   Diagnosis was made of mild sciatica, probably due to tilting of the fifth lumbar vertebra, caused by prolonged and bifurcating transverse process on the left side of the fifth lumbar.   Because of the mildness of the symptoms and comparatively short time of complaint, operation was not advised.

CASE III.—(76806.) S. P. J., male, aged thirty-five years.   Patient came for consultation complaining of distress in abdomen. Clinically, the picture presented was that of a patient with chronic disorder of the gall-bladder.   He complained of stiffness in back and occasional pains down the back of his legs.   He had a right inguinal hernia.   A laparotomy was performed, the gall-bladder drained, and the hernia repaired.   His general health improved, but the trouble in the back continued, compelling cessation from work.   The pain was confined to the right sacro-iliac region, extending down the back of the right thigh and calf, following the course of the sciatic.   There was an increase of pain upon going upstairs or inclines.   Flexion with extended knee caused pain.   No pain on flexion with knee flexed.   Had lost considerable sleep and was nervous.   Roentgenogram disclosed a bifurcated transverse process of the fifth lumbar on the right side (Fig. 201).   A second operation was done, and a portion of this process removed where it was found to impinge on the iliac crest.   For a month or two the patient's condition was much improved, but gradually the symptoms returned, and he reports having as much trouble as before. He had been told by an orthopedist at his home that he has a dislocation of the sacro-iliac and manipulation has been advised (Fig. 202).

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RESECTION OF THE KNEE-JOINT FOR TU-BERCULOSIS *

MELVIN S. HENDERSON

Resection of the knee-joint is an old operation dating back to Filkin,[1] of Northwick, who performed a successful resection in 1762; followed by Park,[2] of Liverpool, in 1782; by Moreau,[3] in France, in 1792; and Mulder,[4] in Holland, in 1809. Buck's[5] operation in 1844 is given credit of being the first in America. In pre-Listerian days the operation was not in favor on account of the frightfully high operative mortality. The statistics of Heineke[6] (1866), reporting 11 cases with 4 successes and 7 deaths, emphasize this fact. Ollier's[7] statistics up to 1870 show a corresponding mortality, he having performed 17 operations with but 1 recovery. After the introduction of antisepsis Ollier's mortality dropped to 10 per cent. To-day, in properly selected cases, the operative mortality may be considered practically nil.

As a functionating knee rarely follows the treatment of tuberculosis of the knee in an adult, ankylosis with cessation of symptoms often is the best result to be hoped for. In an adult, however, tuberculosis *per se* rarely brings about an ankylosis. It may more readily occur after the formation of abscesses and discharging sinuses following secondary infection.

The history of cases in our clinic presenting a bony ankylosis of the joint (Fig. 203) is very different from those cases of the tuberculous type to be considered in this paper. The onset is sudden, coming on frequently as a result of exposure to the cold. Gonor-

rhea may be a cause.   Tonsillitis or sore throat is often a premonitory symptom; chills and fever ensue, and the joint or joints become involved, causing swelling and pain so excruciating that opiates only partially control it.   The patient is usually allowed to assume any posture that gives him greatest comfort.   Symptoms usually subside in from six to twelve weeks.   Ankylosis is apt to occur in the position in which the joint was held during the acute

Fig. 203.—Bony ankylosis, result of acute infection.   Note the tendency of the medullary cavity of the femur to become continuous with the medullary cavity of the tibia.

stage of the disease.   The soreness gradually passes away, the general health returns to normal, but the patient is crippled by the mechanical inconvenience of the limb involved.   This is the type of case which promises the best results in arthroplastic work.

The type of tuberculous cases under discussion gives no such history and presents no bony ankylosis (Fig. 204).   The onset is slight, and trauma may or may not be a definite factor.   Accurate

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statistics are difficult to obtain on this point.   The history records remissions, but never entire freedom from some inconvenience. After years of gradually increasing difficulties many patients request amputation. We have yet to see any joint of this type attain bony ankylosis by treatment under casts and braces unless secondary infection has been a complication.

Fig. 204.—Tuberculosis of the knee in an adult of six years' duration.   Destruction and disintegration of all constituents of the joint.   No evidence of bony ankylosis.

Undoubtedly, some cases of tuberculosis of the knee-joint are cured by conservative treatment in the early stages.   Definite information would be collected if more early cases were aspirated and the guinea-pig test made.   This test has proved to be a great aid in cystoscopic work and should be of the same value in the diagnosis of obscure lesions of the joints.

The question arises, what shall be done with these cases? Conservative measures should be tried for a reasonable length of

time, though in our experience with cases of tuberculosis of the knee-joint in adults resection is usually the final solution.

The selection of cases, or, rather, their preparation for operation, is important. The results are almost always good if the patient is operated on in the quiescent stage. Pain is much less and swelling and edema of tissues followed by sinuses are not so frequent if this rule is adhered to. Extension and rest in bed are probably the best means of quieting the condition.

Generally speaking, since the results are less favorable in patients past fifty than in those between twenty and forty, it is even more important that the former be operated on during the quiescent condition. A disastrous result leading to amputation is very likely to prejudice the surgeon against a procedure which, if done under the proper conditions, gives excellent results.

This paper is based on a series of 37 patients operated on before March, 1913, and whose histories have been subsequently traced. The records of the Mayo Clinic show 66 resections of the knee-joint before that date, but only 37 could be traced. Up to May, 1914, 78 resections had been done for tuberculosis of the knee, with no operative mortality. Only cases have been selected in which, by a review of the history, operative findings and pathologic report were undoubtedly tuberculous. In some the diagnosis before operation had been cleared up by the guinea-pig test. An attempt has been made to classify the symptoms, but such detailed report would be out of place here. The average age of patients in the 66 cases was twenty-seven years; 43 of these were males, 23 were females. The average duration of symptoms before operation was eight years. These patients all came for consultation on account of varying degrees of pain, disability, and deformity. Thirty-seven patients were traced, and of these, 32 may be classed as cured since the functional results were good: 2 returned for amputation, and 3 died. Of the 3 who died, full information could not be obtained. In one the cause of death (four and one-half years after operation) was given as tuberculosis, but without stating the site of the lesion. Two died of tuberculosis of the lungs, one, one and one-half years, and the

other, three years, after operation.   Very encouraging and grate-
ful letters were received from the patients who were cured, many
of whom had gained 40 to 60 pounds.   Practically all were able
to resume their full duties.   Two stated that there was still some
motion in the knee which caused inconvenience and feeling of inse-
curity, but that they were free from pain.   Rather than resect
again, two pieces of bone will be grafted to induce ankylosis and

Fig. 205.—Radiograph of specimen.   Ankylosed knee-joint three years after resection.   Amputation
because of pain and formation of abscesses.

relieve these patients.   Two patients of the 37 have persist-
ing sinuses.   In one case the sinuses persisted even though there
was firm bony ankylosis.   This patient also had pulmonary
tuberculosis.   The abscesses which formed in the region of the
knee, causing pain and loss of sleep, were opened and drained as
they appeared.   Vaccines, tuberculin, etc., were used to no avail.
Three years after the resection amputation was performed and the

patient now gets about on an artificial limb; tubercle bacilli have disappeared from his sputum and the roentgenogram of the lungs shows marked fibrosis. A dissection of the removed joint shows firm bony ankylosis (Fig. 205). Each sinus led down to a superficial bony erosion, practically a tuberculous periostitis. Such sinuses may occur in cases operated upon in an acute stage of the condition.

The time spent by the patient in absolute rest prior to operation is well repaid by the easy and shortened post-operative convalescence. In the acute stages, with threatened rupture of abscesses, it is better to insist upon rest and aspiration of the abscess, which, in a certain percentage of cases, will avert further formation of abscesses and sinuses. Three patients with sinuses were operated on. One of these, operated on in the acute stage in our clinic, had an amputation elsewhere three months later and died of cause unknown. In the two other cases operated on the sinuses healed within four months.

The social status of the patient influences to a great extent the treatment. Obviously, a person of sedentary occupation can more readily put up with the inconvenience of a brace or case than those engaged in active pursuits. The latter will be better off with a stiff knee which allows them to get about without pain than with braces and crutches.

The specimens were examined from a pathologic point of view to see if any definite data could be collected as to whether the primary focus was in the bone or in the synovial membrane. This was impossible to determine, owing to the advanced stage of the disease and the amount of bone destruction. All evidence of the early condition was destroyed, the picture showing only the terminal stage. Ely[8] has stated that the focus is more often primary in the synovial membrane. Stiles[9] has stated that in probably one-half of his cases in children the disease was primary in the synovial membrane. Certainly in our experience it would seem that the majority of cases are primary in the synovial membrane; but this opinion is based principally on clinical and radiographic studies.

All the cases in this series were unilateral. Some had tuberculosis of the lungs when operated on. Definite figures are not possible, for, while many were classified as suspicious, only six were proved to be phthisis. One died which was considered suspicious, and two other deaths occurred three or four years later in patients whose lungs were clearly tuberculous at the time of operation. All were benefited by the operation. Two patients operated on are not in good health owing to kidney lesions, but the condition of their knees is one of bony ankylosis and they are classified among the successful cases. One patient with undoubted tuberculosis of the lungs has gained 35 pounds and reports himself in the best of health. We do not hesitate to do a resection of a tuberculous knee when it is one of two or three foci and seems to be the chief cause of the patient's poor general condition. Ordinarily the patient's finances prevent indefinite treatment by rest and special apparatus. Our object must be to enable these people to get about without pain.

The types of operations suggested for tuberculosis of the knee-joint vary all the way from an erosion to a complete excision. In this study resection only is considered.

Ely, in the last few years, has made a point that the disease in the joint is there because the soil is favorable to the growth of the tubercle bacilli, and that all that is necessary is to change the soil to starve out the bacilli. Therefore he advises removal of only enough of the joint-surface to produce an ankylosis, doing this by aid of a chisel without disturbing the crucial ligaments or spreading wide the joint. The soft tissue may be ignored. The ankylosis changes the spongy bone to hard bone.

The Fergusson[10] type of operation is used in the Mayo Clinic and is essentially as follows: A tourniquet is applied six inches above the knee; an incision is made two-thirds the circumference of the knee, following the line of the joint and running just below the patella, severing the lateral ligaments and the ligamentum patellæ, allowing quick exposure. The leg and foot are wrapped with sterile towels so that the knee may be acutely flexed on the thigh. The soft tissues are dissected back $3/4$ inch from the head of

the tibia and the femur.   If the patella is fixed or seems involved, it is removed.   An amputation saw with a blade three to four inches wide is used to saw off the top of the tibia and femur, usually removing about ½ inch of the tibia and ½ to ¾ inch of the femur.   By a little care the saw may be introduced at such an angle as to insure the accurate fitting of the ends of the bone at the angle desired.   If the patient's business requires much standing, about 10 degrees flexion is desirable, but for those who remain seated much of the time 15 to 20 degrees flexion is a better position. The denuded surfaces are swabbed with iodin, the soft tissues sutured together with chromicized catgut, and a rubber drain inserted.   Such soft tissue is removed as may be superfluous in closing the wound.   An extensive dissection for removal of all the soft tissue showing involvement is not necessary or desirable. Through a separate incision in the skin a wire nail is driven up through the head of the tibia into the femur.   The nail-head is left projecting out through the skin, whence it is very easily removed in two or three weeks.   It serves its main purpose while the dressing is being applied, and in this differs from the use of metal plates, as advocated recently by Osgood.[11]   The tourniquet is removed and the skin is sutured with silkworm-gut and horsehair, and the leg is then put up in a plaster-of-Paris case, including the ankle and foot.   At the same time a window is cut over the wound.   Within forty-eight hours the dressing is changed and the drain removed. Naturally there is some pain, which usually ceases within forty-eight hours, and once bony union has started, the convalescence is free from pain.   The case, together with the suture and nail, is removed in about two weeks, and a new case is applied which remains from six weeks to three or four months.   When the ankylosis seems firm enough, a stiff-legged brace is used by day and a light posterior splint at night.   Some of our patients have had sufficiently firm union to bear their weight in four months, but usually it takes about a year (Fig. 206).

A review of our work has led us to advise the operation in all cases of proved tuberculosis of the knee, even if but slight destruction of bone has been revealed by the Roentgen ray.   On opening

up a joint in which the radiogram has shown but slight destruction of bone, one is often surprised to find complete destruction of

Fig. 206.—Bony ankylosis one year after resection.

the articular surfaces.   In none of our cases of this type has there been bony ankylosis demonstrable upon exposing the joint at operation.

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STUDIES IN THE TREATMENT OF FRACTURES *

MELVIN S. HENDERSON

I. THE TREATMENT OF UNUNITED FRACTURES OF THE TIBIA BY THE TRANSPLANTATION OF BONE

Ununited fractures of the tibia are relatively common, especially in the middle and lower third of the bone. It is true that we do not see cases of such long duration as those of ununited fractures of the humerus, which may be of five and ten years' standing. In one case, recently operated on in the Mayo Clinic, the humerus had been ununited for fourteen years. An arm thus partially disabled is infinitely more useful than an artificial arm, and is not, therefore, sacrificed. On the other hand, an ununited fracture of the tibia necessitates the use of crutches or, for a laboring man, complete cessation of work. In such cases an artificial limb is more useful and, therefore, the legs are sometimes amputated.

The ingenuity of the surgeon has been greatly tried in the treatment of these cases. Many procedures have been advocated, prominent among which, of late years, have been the silver wire and the metal plate. The plate is best suited for certain recent fractures in the tibia in which apposition of the fragments cannot be maintained in any other manner. A perfect anatomic reposition of the fragments is not essential for excellent function. A little displacement is permissible if the axis of the line of weight-bearing in each fragment is parallel, but weight-bearing through an angle is bad, particularly if the fracture be near the joint.

Transplantation of bone into the tibia gives excellent results,

and the method herein described is so simple and reasonable that it must inevitably supersede the use of the plate or other mechanical devices in the majority of cases.*

It was noted in these cases that the fibula when fractured had united. If these patients have been previously operated on, or if there is much laceration of the skin at the time of the accident, the difficulties in operating are greater. This scar, which is closely adherent to the bone, poorly nourished, and deprived of subcutaneous tissue, is liable to slough after being lifted up, a complication which occurred in two of our cases. No infection followed, but careful dressings were necessary after the slough had separated until healthy granulations appeared.

In the treatment of cases of ununited fractures enough bone for transplantation can be obtained from the same leg, thereby greatly shortening the patient's stay in bed. The transplanted bone will live if the following conditions are fulfilled: (1) The observation of asepsis; (2) if bone be obtained from the same individual; (3) securing a free supply of blood in the new habitat; (4) maintaining a reasonable amount of bony contact.

This procedure is not recommended for the infected case, although some surgeons have transplanted bone with infection present and obtained good results. When infection is present, the bone to be transplanted should first be removed from the other leg and all work completed on this leg before the infected member is touched.

The question here arises: When are we to transplant bone for fractures which have not united? Robert Jones† speaks of the condition as "delayed union." This is a better nomenclature than "non-union," since it is probable that all these fractures would unite in time. However, with the present-day advantages of surgery an operation for this condition may be advised, thereby saving time for the individual and an earlier return to his wage-earning capacity.

* In describing this method the author makes no claim for originality. Others have used practically the same procedures. Buchanan published an article and reported a case (International Journal of Surgery, October, 1912).

† Amer. Jour. Orthop. Surg., 1913, xi. 314–335.

There can be no definite period assigned for transplanting bone in these cases of delayed union. Many factors should be considered, but the chief aim of the surgeon is to restore the individual to his duties at the earliest possible period.

There is generally but little deformity in the fractured tibia, and good alinement and position may usually be maintained by the aid of plaster-of-Paris casts or splints. It is difficult to understand why union should not take place in these cases. The type of cases under consideration in this paper does not include the so-called Pott's fracture. Here it is true that the tibia enters into the question, but non-union rarely results, and these patients usually seek relief because of faulty alinement, which so intimately involves the ankle-joint as to demand correction.

The 9 cases herewith reported were all healthy young males —one a boy eight years of age. Syphilis was present in but one, and this was contracted after the leg had been broken one year. In the series of 9 cases 6 were simple fractures and 3 were compound fractures. One of the latter had become infected. The other two, although the bones protruded at the time of the accident, had healed without any signs of infection. It does not seem probable that infection had any bearing on the delay in union.

The bone in these cases is especially adapted to transplantation since it is easily accessible, the operative field being just beneath the skin. The transplant will not have to hold the alinement, because this can readily be done by external means. The fibula, which is intact or firmly united, maintains the length of the limb and no slipping-by of the fragments is likely to occur. The transplanted bone may be placed in a normal field; it is not necessary to put it in the medullary cavity. A gutter is chiseled or sawed in the fragments down to the medulla, thus allowing the transplant to have a natural bed to rest in. If a piece of cortical bone is used as a medullary plug, it acts merely as a foreign body. It is, however, an absorbable foreign body and gradually disappears. During its absorption osteogenesis is promoted which leads to union. In operating on cases of ununited fractures of the humerus twenty-five years ago, C. H. Mayo used an ordinary

cataract bone knife-handle to make an intramedullary plug. He fastened linen sutures to its center, leaving long ends, and brought these out through the wound. These sutures were tracted every day, thus causing a little motion of the plug. In this way a mild irritative osteitis was kept up which was conducive to osteogenesis and the formation of callus. This ivory plug usually healed in, but occasionally disintegrated and came out in small pieces.

If transplants are taken from the opposite tibia, patients must be kept off their feet for a month or more. It is much simpler to take the bone from the same tibia, either above or below the fracture, and get our patients up within a few days. The bone should preferably be taken from the flat internal surface of the tibia rather than from the crest, which is dense, strong, and being the apex of a triangle, serves a most important weight-bearing function. A piece of bone removed from here down to the medullary cavity weakens the bone out of all proportion to the size of the piece removed. The bone on the internal surface is not so dense and is also more vascular, and a large piece may be removed here without greatly weakening the bone. All the layers, *i. e.*, periosteum, cortex, and medullary lining, should be included in the transplant.

In studying these pieces of transplanted bone by a series of roentgenograms after their implantation it is apparent that they live and functionate without being replaced by new bone. In the tibia, by forming a gutter down to the medullary cavity, the transplant can be placed so that periosteum meets periosteum, cortex meets cortex, and medullary lining meets medullary lining, thus obtaining an anatomic approximation favorable to rapid healing.

The technic of the operation, as followed in our more recent cases, is simple and may best be shown by the diagram (Fig. 207). Either by the aid of the chisel or the motor-propelled circular saw (Fig. 208) a piece of bone is removed from the internal flat surface of the tibia. The bone should be of sufficient length to make a substantial bridge, usually two or three inches long and about $\frac{1}{2}$ inch in breadth, and should include all the layers. This is taken from the longer fragment. A piece the same width in the same
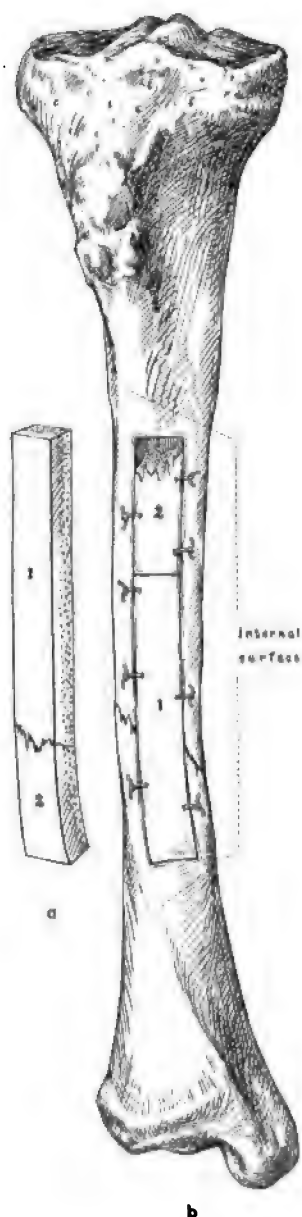
Fig. 207.—1, a, Shows diagram of transplant removed from the long fragment; 2, a, shows transplant removed from the short fragment. 1, b, shows inversion of long transplant to bridge fracture; 2, b, shows short transplant inserted to fill gap left by removal of transplant from long fragments. · Catgut sutures in periosteum of graft and shaft.

line is then removed from the smaller fragment. This is saved. The larger piece of transplant is then inverted so that sound bone will bridge the line of the fracture. The part which was the upper end fits into the angle distal to the fracture in the smaller frag-
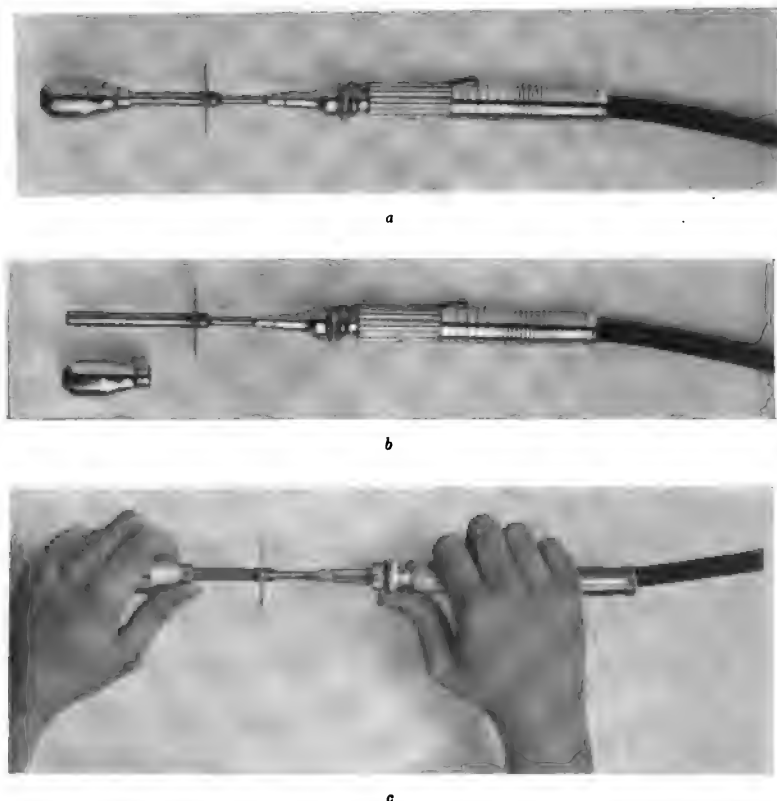
Fig. 208.—*a*, Type of circular saw used. Note removable metal cap on distal end of shaft. In using the saw, the tip of the shaft which fits into this cap should be greased with sterile vaselin to prevent it becoming too hot to hold. All the metal can be dry sterilized. The flexible shaft is wrapped with a sterile bandage. *b* shows metal cap removed. *c* shows method of holding saw, which gives the operator easy control

ment. The piece removed from the smaller fragment is then used to fill the remaining gap in the longer fragment. Both pieces are sewed in by stitching the periosteum of the transplant to the periosteum of the shaft. The skin is then closed with silkworm-

gut and horsehair and the dressing applied. A plaster-of-Paris cast is applied to include the knee and ankle. This is removed at the end of two weeks. Sutures are removed and a new cast put on which is left for from four to six weeks. Further treatment is guided by the individual case. Union is usually firm enough to permit walking in from three to six months.

CASE A71534.—Roentgenogram 16559. Male, aged thirty-one. Mining engineer. Date of examination in Mayo Clinic, August 2, 1912. Twenty-six months previous to examination the man had sustained a compound fracture in the lower third of the tibia and fibula. No infection followed. In spite of good treatment by cast, splint, and brace, there was but little union and that was fibrous. In October of 1911 he contracted syphilis, which was treated promptly and effectively. At the time of examination in our clinic, although he had had no treatment for two months, his Wassermann was negative. He was walking with the aid of a brace but had been unable to resume work.

Operation.—On August 12, 1912, the fracture was exposed and a transplant was moved down from above to bridge the fracture. Healing by first intention followed, and the patient was dismissed. Three months later he wrote that the union was firm and asked permission to bear weight on his leg. This he was advised to do gradually.

CASE A78083.—Roentgenogram 18621. Male, aged thirty. Farmer. Date of examination, January 3, 1913. Patient presented himself for examination because of delayed union of a compound fracture of the left tibia of one and one-half years' standing. Infection followed and he was quite ill for two months. At the time of examination in our clinic there were no signs of infection. He had been treated by splints and casts. The union was entirely fibrous, there being free motion at the site of the fracture, and he was using two crutches (Fig. 209).

Operation.—On January 6, 1913, the fracture was exposed and a piece of bone four inches long transplanted from the middle third of the same tibia to bridge the fracture (Fig. 210). Healing occurred by first intention. On May 15th the patient resumed his full duties on the farm. Probably firm union had existed for six weeks prior to that time.

CASE A78224.—Roentgenogram 18668. Male, aged twenty-eight. Miner. Examination, January 7, 1913. Delayed union of

Fig. 209.—Ununited fracture of lower one-third of left tibia, one and one-half years after injury

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Fig. 210.—Shows transplant used to bridge fracture in one of our early cases. The transplant was removed from the crest of the tibia and not from the internal flat surface.
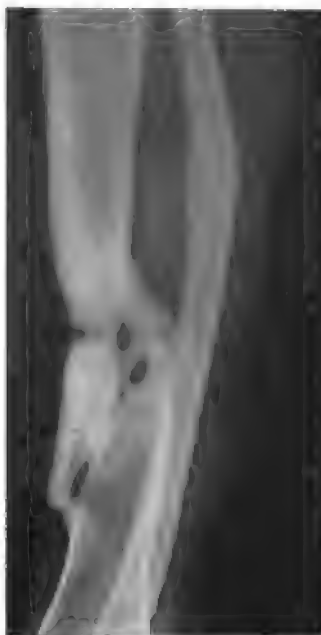
Fig. 211.—Non-union after one and one-half years.
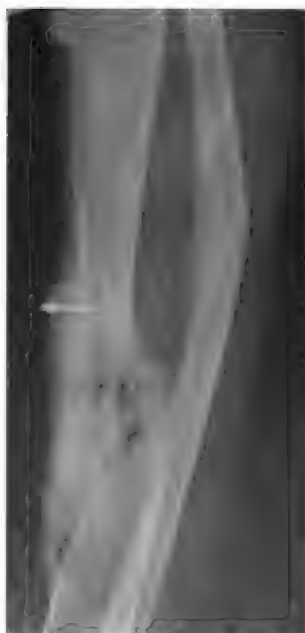
Fig. 212.—Shows transplant used to bridge the fracture. Silver wire was used, contrary to our late technic; also the transplant was removed from the crest and not from the flat internal surface.

fracture of the middle third of right tibia, one and one-half years' duration. There was free motion at site of fracture. Two crutches were used. Amputation had been advised by home physicians.

Operation.—On January 9, 1913, bone was transplanted from the same tibia to bridge the fracture. Instead of using catgut as usual, aluminum bronze wire was used. A scar which was the result of the original accident sloughed after being lifted up at the operation. Under alcohol dressings this surface granulated and healed without infection. The patient did not resume his full duties until September 2, 1913. He wrote that the leg was strong before that time, but he was afraid to use it. A medicolegal question in this case may have prolonged the convalescence.

CASE A80259.—Roentgenogram 19480. Male, aged thirty-two. Laborer. Weight, 200 pounds. Examined in the Mayo Clinic February 19, 1913. One year previous he had sustained a simple fracture in the upper third of left tibia. There was delayed union, and at the end of six months the fracture was wired, but without resulting union. When he came for examination he was still using two crutches.

Operation.—On February 22, 1913, a transplantation was done on the same tibia to bridge the fracture. Primary healing followed, and the patient was dismissed with a leather-sheath brace and crutches. On May 11, 1913, he slipped, throwing all his weight on the fractured leg. There was an injury, and he returned for treatment. The roentgenogram disclosed a new fracture which had occurred at the point where the upper end of the transplant had been removed. The old fracture was intact. A plaster-of-Paris cast was applied. The patient resumed his work on November 20, 1913, and reports the leg solid and straight.

CASE A82916.—Roentgenogram 20710. Male, aged thirty-four. Laborer. This patient was examined April 16, 1913. Nine months previous to the examination he had sustained a simple fracture in the middle third of the right tibia and fibula. Casts and splints were used. After four months he was operated on for delayed union by his home physician. Silver wire was used. No union resulted, and his physician referred him to the Mayo Clinic for treatment. He was on crutches.

Operation.—On April 19, 1913, the fracture was opened and a portion from the same tibia transplanted to bridge the fracture. Primary healing occurred. On October 27, 1913, the patient

resumed his full duties, and in a recent letter stated that he had walked ten miles.

CASE A82640.—Roentgenogram 20553. Male, aged eight. Date of examination, April 9, 1913. Five and one-half years previous had sustained fracture of the middle third of the right tibia. Malposition and imperfect union resulted. Two years ago he sprained his right ankle, and the roentgenogram disclosed nonunion of the tibia. It was wired, but no union resulted. In August, 1911, a Lane plate was applied, but infection followed, and in November, 1911, the plate was removed. Following the removal of the plate the leg seemed to become perfectly straight and quite solid, but at about the eighth month, though the leg was straight, there was motion at the site of the fracture. The union became gradually weaker, with more motion, and the deformity steadily increased. High shoes had been worn to come up over the fracture for more than a year.

Operation.—On April 9, 1913, bone was transplanted, the transplant being obtained from the same tibia. There was a slough of the skin, the result of the poorly nourished old scar, but no infection occurred, and the patient's recovery was uneventful. A recent letter states that he is running and playing without any support and the leg seems perfectly solid.

CASE A87500.—Roentgenogram 22915. Male, aged thirty-two. Farmer. Examination July 9, 1913. On May 12, 1913, he sustained a compound fracture of the left tibia and of the middle third of the fibula. No infection followed. No union other than fibrous occurred. The fibula had united.

Operation.—On July 11, 1913, bone was transplanted from the same tibia to bridge the fracture. The healing and convalescence were uneventful. The patient resumed full duties by November 1, 1913, the leg being perfectly firm and solid.

CASE A89982.—Roentgenogram 22221. Male, aged forty-eight. Farmer. Examination June 16, 1913. Two months previous had sustained fracture of the lower third of the left tibia. There was slight anterior displacement of the lower fragment and non-union.

Operation.—On July 17, 1913, a transplantation was done from the same tibia to bridge the fracture, which was comminuted. A letter from the patient dated December 11, 1913, states that he is walking with a cane. The convalescence was slow in this case, largely because of trauma at the time of the fracture. There was

much swelling of the soft tissues, even two months after the fracture occurred.

CASE A97369.—Male, aged twenty-two. Chauffeur. Examined December 17, 1913. On November 25, 1911, he fractured lower third of right tibia and was treated by splints, casts, etc., until May, 1912, when an operation was performed. Bone transplant and silver wire were used. No union resulted.

Operation.—On December 23, 1913, in the Mayo Clinic a piece of bone four inches long was removed from the middle third of the tibia and used as a transplant to bridge the fracture. The wound healed by first intention.

II. OPERATIVE TREATMENT OF DELAYED UNION OF FRACTURES*

Although there are no dependable statistics on the relative frequency of non-union as compared with normal union in the total number of fractures, still in general practice non-union is rare. During the last four years 181 patients having fractures of one or more of the long bones were examined in the Mayo Clinic. They came for various reasons, such as pain, deformity, limp, sepsis, non-union, disability, etc. There were 68 cases of non-union, and only these will be considered in this paper. Of these, in 31 cases transplantation of bone was done to induce union. Practically all were operated on during the last two years.

The term delayed union is sometimes preferred to non-union, but it is impossible to state arbitrarily just when a delayed union becomes a non-union. Undoubtedly the majority of these fractures would ultimately unite, but for reasons both economic and psychic it is important to restore the patients to their normal productive condition as early as possible. Our records show that non-union existed as much as two, three, and fourteen years respectively after the fracture was sustained.

Not all cases of delayed union should be subjected to operation. The patient and the surgeon should have the choice of the various

methods of treatment, which choice will necessarily be influenced by the surgeon and the armamentarium he has at his command.

Jones[1] calls attention to the Thomas dam method, which consists in pounding the area over the fractured ends with a padded mallet and damming up the blood by a rubber tourniquet applied three or four inches above and below the bone ends. The same author calls attention to those cases of malunion having a certain degree of non-union, in which there is an abundance of callus and tenderness over the callus. The fragments of the bones are usually easily manipulated into line, and, once proper line is established, the callus hardens and firm union takes place more readily. Gerster[2] and Lyle[3] have drawn attention to the method, used in Bier's clinic, of injecting the patient's own venous blood between the fractured ends. The metal plate has been and still is freely used in the treatment of non-union, but some authorities claim that the presence of the metal occasionally retards rather than favors union. Lane[4] obtains beautiful results by the use of these plates, and attributes them to patience and care in the maintenance of asepsis. In speaking of recent fractures he says: "I believe that for some time the results that will be obtained by operation on simple fractures will at least be as hopelessly unsatisfactory as are those following non-operative treatment. Indeed, some surgeons seem to regard as normal the necessary removal of screws and plates by a process of suppuration, and are inclined to consider the infection as resulting from the presence of organisms in the blood rather than from their own insufficient precautions."

In advising operation, the age, occupation, and constitutional condition of the patient should be considered. It must be remembered that the method, be it bone transplantation, wiring, freshening the ends, or plating, is to be employed to unite the fracture, and that the fracture is not to be used to exploit the method. It has been the custom in our clinic carefully to handle cases of fracture of the femur and not subject them to prolonged operation or to severe procedures in an attempt to obtain lengthening by traction. Many attempts to secure lengthening in old fractures with shortening of muscles, nerves, and vessels have resulted disastrously, as

mentioned by Martin.[5]   We have, therefore, more often used the metal plate on the shaft or nailing of the neck rather than bone transplantation, since they are more rapid.

Bone transplantation to the surgeon is an attractive procedure and gives success in a large percentage of cases of non-union.   It is not infallible, and certain laws must be adhered to.   Asepsis must be maintained, although occasionally bone-grafts have healed in the face of infection.   The piece of bone used as a transplant should be from the same individual, and should be assured of adequate bony contact in its new bed, so that it will be readily nourished. The inlay method, as advocated by Buchanan,[6] Albee,[7] the author,[8] and others, has points in its favor over the intramedullary method as used by Murphy.[9]   By this means an anatomic approximation of parts may be obtained, whereas in the intramedullary method the bone plug is in a field not normal to it, and is treated by nature as a foreign body and gradually absorbed.   It stays long enough, however, to act as a splint, and in absorbing induces a freer blood-supply and so induces osteogenesis.   That the intramedullary method is highly efficient is shown by the work of Murphy, but in our clinic it is not depended upon alone to secure union, but we use either the inlay method alone or combine it with the intra-medullary.

There were 16 cases of non-union in the tibia.   The time during which non-union had persisted averaged 12.2 months, the longest period being twenty-six months and the shortest two months.   All were males, and the ages varied from eight to fifty-five years.   We are now advising transplantation of bone earlier than formerly in cases which seem to be at a stand still (Figs. 213 and 214).   Generally speaking, functional results are more quickly secured by operation in cases in which non-union has persisted for but a few months than in those in which it has persisted for many months.   The greater degree of osteoporosis in the long-standing cases produced by the lack of use of the leg and by its fixation may in some degree explain this.

Seven of the 16 cases had been previously operated on one or more times.   In some, silver wire had been used; in others, the

Lane plate, and in two bone grafting, had been done.   One had
had an intramedullary bone plug applied elsewhere.   One had
been operated on by the inlay method in our clinic.   This patient
was recently reoperated on in our clinic.   The case is of particular
interest, since there were two fractures of the tibia, one in the
upper and one in the lower third.   The one in the upper third had

Fig. 213.—Fractured tibia, eighteen months' non-union.

a marked malposition, and we operated on it first, intending to use
a bone graft, but found that it was held more readily by a Lane
plate which was applied.   Union resulted, but at the end of three
months the metal plate had to be removed on account of a serous
discharge.   At the end of six months no union was evident in the
lower third fracture, and bone transplantation was done, the bone

being obtained from the same tibia.   At the end of nine months
more there was no union and bone transplantation was again per-
formed, this time the bone being obtained from the opposite tibia.
The patient is still under observation, only three weeks after
operation, so we cannot say what the result will be.   It is certain
that the bone obtained at the first transplantation was not of

Fig. 214.—Same as Fig. 213, six weeks later.   Complete restoration of function in three months from
time of operation.

normal structure, as the leg had then been in a cast for one year.
In this type of case it probably is better to remove the bone from
the opposite tibia if sound.

The scar, often quite pronounced in cases previously operated
on, causes a little worry during the healing after transplantation.
It may be densely adherent to the bone, and devoid of the normal

subcutaneous tissue which allows the skin to move. On dissecting up the flaps for the necessary exposure the blood-supply is occasionally interfered with, so that they slough. This happened in several of our cases, but by careful alcohol dressings the wounds granulated in satisfactorily and the grafts were not lost.

Time will not permit mentioning the many interesting features in these cases, but I should like to cite one—a case of a boy eight years of age. When he was two and one-half years old he fractured his right tibia in the middle third. Healing in malposition occurred, with what must have been strong fibrous union, as the parents said there was always some motion. Three and one-half years later he hurt the leg. Radiograms showed no union, and clinically there was increased mobility. He was operated on elsewhere in 1911, and the fragments wired, but no union resulted. In August, 1911, a Lane plate was put on, infection ensued, the plate was removed, but following this the leg seemed to get perfectly straight and quite solid. Six or eight months later, though the leg seemed straight, there was motion at the site of fracture. This weakness and mobility had gradually increased up to the time of our first examination, April 9, 1913. Three days later a bone transplantation was performed with normal convalescence. The patient was examined on June 20, 1913, and pronounced cured. He returned in June, 1914, with a fracture at the lower end of the bone graft. Under casts union has again occurred. This case illustrates the odd behavior of fractures in children, and suggests in some degree the peculiar fractures occurring in osteitis fibrosis cystica.

Why non-union occurs in apparently healthy people we cannot say. In our series syphilis seems to have had no bearing. Robinson[10] favors the view that non-union may be due to a thrombus in the nutrient artery, since it is more likely to occur in the upper or middle third, where the nutrient artery enters. If this does occur, the impaired nutrition may interfere with the bone repair, so that connective tissue is interposed and forms a permanent block to the bridging across the gap by the Haversian system of osteoblasts. In our 16 cases there were 6 of non-union in the lower third, 9 in the middle third, and 1 in the upper third.

Strictly speaking, in our series of 16 cases there was but 1 in which union failed by this method.

There were 7 cases of ununited fracture of the humerus treated by bone graft—4 in the middle third and 3 in the lower third.   Six of the patients were males and 1 female.   Their ages were from eighteen to sixty years.   That non-union may persist almost indefi-

Fig. 215.—Type of fixation for fractures of the humerus.

nitely is shown in one of our cases of fourteen years' standing. A study of these 7 cases emphasizes the point that fixation is necessary after the transplantation of bone, and that probably the best fixation method is that obtained by a plaster-of-Paris cast encircling the thorax, taking in the shoulder, elbow, and wrist on the affected side.   A window may then be cut to allow dressing of the wound (Fig. 215).   Three of the 7 have been treated by the intra-

medullary method and 4 by a combined intramedullary and inlay. One of the grafts broke where post-operative fixation was inadequate (Figs. 216 and 217). One graft was lost where there was already infection at the time of operation. Contrary to a previously expressed opinion, in the case of fourteen years' standing there was firm union in three months (Figs. 218 and 219). In this case there

Fig. 216.—Non-union in the humerus one year after accident.

was no osteoporosis, as the man had been using the arm freely even with pseudo-arthrosis present. A musculospiral paralysis had slowly developed during the last three months. This gradually cleared up after the operation. Two other patients seen since dismissal have firm union. Two have been lost sight of, and 2 others, 1 one year and 1 eight months after operation, still have ununited fractures, though they are improving. Both of

these had had compound fractures with ankylosis of the elbow-joint. There are then only 3 cures in this group. These all had fixation by plaster-of-Paris casts, whereas the others did not.

We have had 4 cases of non-union in the forearm treated by bone transplantation—2 males and 2 females, aged eleven, twenty-

Fig. 217.—Fracture of graft two months after operation, probably due to patient having stiff elbow and inadequate fixation after operation.

three, twenty-seven, and twenty-eight years. Of these, one, a girl of eleven, has secured no union. Our Wassermann test in this case was negative, but previously had been elsewhere reported repeatedly positive. Operation was done eighteen months ago. This case further emphasizes the difficulty of obtaining union in

many of the cases of non-union in children. The bone in this
case was obtained from the tibia. In 3 cases the bone was ob-
tained from the longer fragment of the bone involved. Two cases
have not been heard from. One other failed to obtain union until

Fig. 218.—Non-union of fourteen years' standing. Note the density of the bones. Patient had used the arm in spite of the pseudo-arthrosis, and came for consultation more on account of a slowly developing musculospiral paralysis than the non-union.

a piece of bone was taken from the tibia, when union resulted.
Two were in the ulna and two in the radius.

In the femur transplantation of bone has been used 4 times—3
times in ununited fractures of the neck of the femur and once in the
shaft. All were males, aged from twenty-seven to forty-nine
years. In our cases of recent fracture of the neck of the femur

good results have been obtained by the Ruth-Maxwell method of
traction and counterextension. Whitman[11] reports good results
by his method of forced abduction.   In this group certainly some
technic is needed which will give better results than were hereto-
fore obtained.   We have used screws and nails successfully for

Fig. 219.—Same as Fig. 218.   Firm union three months after operation.   Musculospiral paralysis en-
tirely disappeared and full function restored.

ununited cases, but the transplantation of bone seems to be a more
surgical procedure.   Albee[12] has used the bone plug driven through
the trochanter into the head of the bone and reports success.   We
have tried this in two cases of non-union.   One was a man forty-
nine years of age with non-union after one year, and the other was

Fig. 220.—Non-union, fracture of the neck of the femur of one year's duration.

Fig. 221.—Bone plug in position.

Fig. 222.—Same as Fig. 221, three months later. Fracture of bone plug.

Fig. 223.—Painful non-union of one year's duration

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a man of thirty-nine years of age with no signs of union ten weeks after the accident.   In both of these the bone plug broke, as illustrated in the radiograms (Figs. 220, 221, 222).   Accordingly in our next case we took a piece of bone from the tibia four inches in length and cut it into two pieces.   The incision was made over the hip, the exposed surfaces cleansed of all fibrous tissue, provid-

Fig. 224.—Patient operated on; union secured in three months by wedging in two small pieces of bone after exposure of the fragments.

ing fresh raw bony surfaces.   The short pieces of bone were then packed in between the surfaces and the leg abducted and put up in a plaster-of-Paris spica extending from the chest to the toes.   In three months firm union was secured, whereas there had been painful non-union for over one year prior to the operation (Figs. 223 and 224).

The case in which the bone in the shaft of the femur was used was a fracture of the lower third which had been sustained over a year before. It had previously been plated, but failed to unite. A piece of bone 8 inches long was removed from the tibia, cut in two, and both portions used to bridge the fracture by the inlay method. This was done recently and healed by primary intention, but, as yet, nothing can be said about the success of the transplantation.

Out of the 31 cases, 4 cannot be reported upon since they have not been traced. In 6 cases, for some reason, the fractures have not united, probably because in the case of fractured tibia poor bone was used as a transplant; in the 2 cases of fractured humerus there was lack of adequate fixation, both having stiff elbows in an extended position; while in the cases of fractures of the neck of the femur the failure of the bone grafts was due to an insufficient amount of bone being placed in the fracture line.

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III.   END-RESULTS IN FRACTURES*

The end-results of fractures is rather a wide subject, and it is impossible, in a brief paper, to touch on more than the chief points of interest.   Each man's ultimate results in the treatment of fractures of the long bones vary according to the material which comes to his hands.   The surgeon who has the care of a large number of men occupied in an industrial plant entertains a more optimistic view of the treatment of fractures than does the orthopedic surgeon.   The former's patients are strong, hearty, vigorous men, in the prime of life, who are, as a rule, excellent subjects for treatment.   One of the conditions which may cause complications is alcoholism.   In the main, however, under ordinary surgical care and treatment satisfactory results are attained.   An orthopedic clinic shows a very different picture.   The patients present the end-results of fractures, but they are all poor results, and the surgeon dealing with these cases acquires a pessimistic point of view.   These patients all come complaining of their old fractures.   It may be pain, due to various causes, non-union, disability due to extreme deformity, subsequent osteomyelitis, paralysis, etc.   The body of truth lies somewhere between the views of these two groups of surgeons.   We must not satisfy ourselves with our results, but must ever try to obtain better results.   In the Mayo Clinic we naturally see the bad results.   Our material is of the type ordinarily seen in an orthopedic clinic.   In our immediate territory there are no large industries which lead to many traumatic injuries, and our number of recent fractures is not large.   From a study of a series of these old fractures we can recognize such as are commonly bad end-results, how possibly to avoid them, and the way to restore function to the limbs.

In reviewing over 180 records of bad end-results in fractures we find that 23 may be classified under the elbow, 67 under the tibia and fibula (30 coming because of non-union and 15 because of ankle-joint involvement), 25 under the humerus, and 45 under

the femur. These fractures had all been treated by different men in different places and under varied conditions. Many of them were undoubtedly the best result attainable under the circumstances, but it would seem as though a better result could have been assured in a considerable number if more care had been exercised at the first setting and if there had been more painstaking after-care. I cannot enter into a discussion as to whether or not the so-called operative or conservative treatment should have been followed.

In 1912 the British Medical Association[1] appointed a committee on fractures, and with great care this committee put forth a report on the end-results, based on 2940 cases. Every person whose case formed a part of the report was seen and examined by a member of the committee. In no case was the report made by the surgeon attending the patient. There were 2596 cases treated by non-operative measures, with 70.4 per cent. good functional results, while in the 147 submitted to primary operation 79.5 per cent. good functional results were obtained. Robert Jones[2] says: "Taking all the statistics together, they prove that if the anatomic result is good, the functional result is good in 90.7 per cent.; while if the anatomic result is bad or moderate, a good functional result is obtained in only 29.7 per cent." The committee makes this statement: "For surgeons and practitioners who are unable to avail themselves of the operative method the non-operative procedures are likely to remain for some time yet the more safe and serviceable."

I will briefly consider some points emphasized by a review of our patients coming on account of bad end-results.

Non-union or Delayed Union.—Experimental work has shown that actual bony union is rather slower than our text-books would lead us to believe (Fig. 225). Eighty-three days is an early date for complete bony union in animals, and it is usually one hundred and fifty to one hundred and seventy-five days. Allison and Brooks,[3] in their studies on ankylosis, show that ankylosis occurs by stages: (1) union by granulation; (2) union by fibrous tissue; (3) union by cartilage, and (4) union by bone. Their experiments were

performed on epiphyseal bone, but point out the necessarily slow process.   Many of our patients have told us that ankylosis seemed fairly firm at the end of six or eight weeks, but that under repeated examinations the union became less firm, and on walking it rapidly decreased.   In many a pseudo-arthrosis persisted.   In one humerus thirteen and one-half years, and one tibia eight years, had

Fig. 225.—Condition six months after fracture.   No evidence of union.

elapsed from the time of the original injury.   In some, for an unknown reason, non-union persisted for months, even under adequate fixation.   The fact that the fracture was compound did not seem to have any bearing nor, in our cases, was syphilis responsible.   It would seem to us then very important that we should remember this somewhat slow and complicated process of

repair in fractures, and that we should prolong our fixation to suit the individual case.

Fractures of the Neck of the Femur.—Several points of interest can be brought out by a review of these cases. A study of recent writings would lead us to believe that the abduction method of Whitman[4] is a method of choice where possible. The traction method, called the Ruth-Maxwell method, also seems to have given excellent results. These patients, as we have seen them, have been cases of one to three years' standing, and came to us on account of disability, pain, and shortening. Many of these were not diagnosed at the time of injury. The history is that of a fall followed by severe pain and disability. No crepitus is to be elicited, no shortening is demonstrable at that time, no eversion of the foot, and a diagnosis of sprain and contusion is made. After three or four weeks these patients are encouraged to walk, although protesting, often bitterly. No further physical examination is made by the first physician and no roentgenogram taken. Another physician is called, shortening of one-half to one inch is found, x-ray examination advised, and fracture of the neck of the femur shown. An absorption of the neck has gradually occurred, with consequent deformity (Fig. 226). This is a common history as we take it. Many times in old people, because of age and constitutional weakness, the "let alone" treatment is the only one possible. A bad result is thus anticipated, the patient and relatives warned, and no consequent blame falls on the practitioner. These patients as they present themselves, with their disability, pain, and shortening, are a difficult group to treat. If their general condition warrants, an operation, either by nailing or bone-grafting, is advisable. We have in the last six months operated on a few of these cases by exposing the joint by the Murphy incision and lifting up the tip of the trochanter with its attached muscles. The capsule is opened, and the fractured surfaces freshened. A piece of bone six inches long and one-half inch wide is removed from the flat internal surface of the tibia and cut in three pieces, each two inches long. These are then placed side by side from above downward, inside the capsule, and in a measure help to

restore the neck of the femur and bring about a bony union. One case of non-union of fifteen months' standing has been restored to function by this method.

Shaft of Femur.—In our clinic many cases of fractures of the shaft of the femur have been operated on by using a metal plate. These patients volunteer the information that up to the time their surgeon permitted them to commence weight-bearing the leg was straight. We are misled in these cases by the apparently
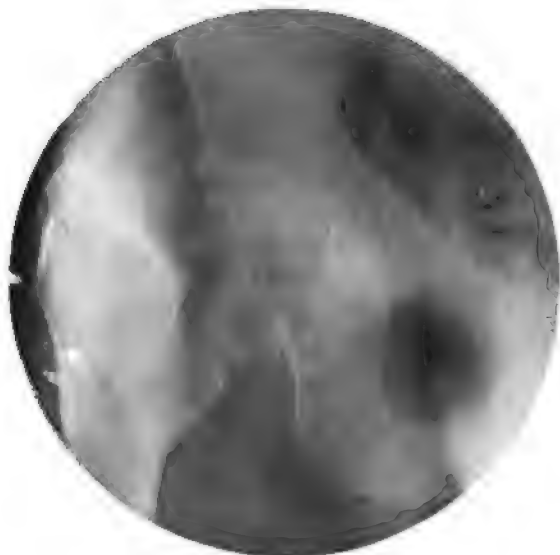
Fig. 226.—Fracture of the neck of the femur showing the marked absorption of the neck.

firm union after three months (Fig. 227). By all examinations—manipulation and *x*-ray—the limb seems solid. Bowing occurs on beginning to use the leg. Once this bowing occurs and use is persisted in, a weakening of the callus between the fragments occurs and pseudo-arthrosis of varying degrees results. A large callus is thrown out, but this is a frantic attempt on the part of nature to bring about union. If at the first sign of bowing the leg were forcibly corrected under anesthesia and immobilization carried out for another three to six months, solid union would occur.

Fractures of the Ankle (Pott's Fracture).—In our series 15 bad results were seen following the so-called Pott's fracture. The name here is used in its broadest application. These patients practically all complained of pain and disability on account of the valgoid deformity (Fig. 228). I cannot do better than quote Robert Jones[2] again here, who states: "The crux of the matter

Fig. 227.—Fracture of shaft of femur. Bowing after operation. Non-union persisting in spite of large callus.

lies not in the fracture of the fibula, but in the outward and backward dislocation of the foot. . . . Every surgeon in reducing such a fracture endeavors to invert the ankle, but comparatively few take any measure to maintain inversion of the foot after the patient begins to walk." These cases of eversion of the foot are not due to poor setting, but when the patient begins to

walk without any support two months after the fracture, the callus yields and valgus deformity appears.   After Jones' method, I have made it a routine procedure to raise the inner side of the sole and heel and provide an outside iron and inside T strap (Fig. 229).

Fig. 228.—Outward displacement of astragalus following fracture at ankle causing valgoid deformity.

Fractures of the Elbow.—Following fractures in the region of the elbow marked loss of function may result, due to limitation of motion.   The report of the British Medical Association showed 40 per cent. poor end-results.   Hitzrot[5] reports 52 successes out of 53 cases where the external condyle of the humerus was involved—a very good showing, and probably to be accounted for by the fact that the hyperflexed position was used.   Practically

all fractures in the region of the elbow-joint with the exception of those of the olecranon are best treated by this position of acute flexion and supination. Limitation of flexion in these elbow-joint cases is due to exuberance of callus and to traumatic arthritis. With the coronoid process of the ulna and the head of the radius

Fig. 229.—Inner side of sole and heel raised, outside iron and inside T-strap to produce slight eversion of the foot.

pushed up against the lower end of the humerus, the formation of callus in this direction is limited. Passive motion is a frequent cause of excessive callus formation and loss of motion. We have frequently had patients come with lack of motion in elbows following fractures who gradually recovered very good function by stopping all attempts at passive motion and putting the arm at rest

in acute flexion for two weeks, and then allowing only moderate
active motion.   Reduce the sensitiveness of these joints, and sur-
prisingly good results will be obtained.   This point has been
emphasized by Jones[6] for years, and Gillette,[7] in a paper, lately
has drawn our attention to it.

The striking point in a review of these cases of bad end-results
is not that the primary care was poor or inefficient, but that the
after-care was not controlled or carried out with the fixed purpose
of treating each case as a law unto itself.   Insufficient time allowed
for fixation was the usual cause of the non-unions.   Once a promis-
ing callus-formation has been abused or broken down, either the
union is greatly delayed and a false joint persists indefinitely or
malunion occurs.   Needless to say, in many instances the patients
themselves were unruly and did not follow instructions, but this
does not alter the fact that the after-care is more often the cause
of poor results than the primary or active care.

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TECHNIC

CHOICE OF METHODS IN THE REMOVAL OF THE EYEBALL *

CARL FISHER

There are four classic methods in general use by which the eyeball may be removed: (1) Simple enucleation; (2) enucleation with the insertion into Tenon's capsule of a prosthesis (glass or gold balls, fat, or paraffin); (3) evisceration, and (4) evisceration with the insertion of a prosthesis into the scleral cup. All these methods have been elaborated by various surgeons, mainly through the introduction of relatively unimportant points of technic. The layman judges the operator's skill largely by the movability of the resulting stump, and hence of the artificial eye worn later. The surgeon must consider also the efficacy of the chosen method in the prevention or cure of sympathetic ophthalmitis, and the possibility of the resulting stump itself becoming a source of danger or irritation to the patient.

The indications for the removal of the eye and the technic of the operations need not be considered here in detail, since they are amply treated in text-books, but I wish briefly to present the conclusions that seem warranted by our experience regarding the indications for each of the above operations.

Simple Enucleation.—This operation has certain good points which should not be overlooked. It gives little postoperative swelling and pain; there is no danger of the stump giving rise to sympathetic ophthalmitis; and it can be done almost painlessly under local anesthesia, though in the young or in nervous people a general anesthetic is preferred. Once healed, the stump seldom

gives rise to pain or other complications, such as the extrusion of a prosthesis, hence the patient can be dismissed in a few days and need not be within reach of medical care thereafter. Unfortunately, the movement of the glass eye may be very faulty, though by no means always; still the risk is considerable in patients likely to be particular about their appearance. The indications for simple enucleation rather than other methods may be summed up as follows: (1) Intra-ocular growths or tuberculosis. (2) A painful blind or shrunken globe. (3) When sympathetic ophthalmitis is believed to be threatening or is actually in process of development. This is for the surgeon's defense rather than that it is a surer protection against sympathetic ophthalmitis than evisceration. (4) In laboring-men otherwise seriously injured or anxious to get back to work. (5) A badly lacerated globe. (6) Panophthalmitis with cellulitis of the orbit. The supposed danger of causing meningitis is not supported by careful criticism; on the other hand, it affords good drainage to an orbit tensely infiltrated.

There are one or two points of technic suggested by recent writers which may be mentioned. Freeland Fergus first cuts the external rectus, leaving a good stump; then rotates the globe strongly inward, thus bringing the nerve within easy reach. He cuts the nerve and continues the rotation, bringing the globe out of the orbit feet first, then cuts the muscles close to the sclera from behind. He uses no hook, but does the whole operation with scissors. This is a very rapid and neat technic and leaves a clean-cut stump. Meller states that in Fuchs' clinic no suture is used. I know by experience that this gives the smoothest stump, totally avoids the little knob so likely to form at the center, with quicker healing and less reaction than as if a suture were taken. The motility of the stump is quite as good as where elaborate pains are taken to suture the muscles together. A purse-string suture should always be avoided, since it gives rise to a tightening of the lateral folds of conjunctiva and very often to a central knob. A point of technic recently broached consists in the use of a snare to cut the optic nerve and vessels after the muscles have been well freed. This causes less bleeding than the ordinary removal with

scissors. I have never seen a serious hemorrhage after enuclea-
tion.

Local anesthesia may be used in the majority of cases—pre-
ferably 0.5 per cent. novocain. The subconjunctiva should be
well infiltrated, then the needle driven back of the globe, so that
the apex of the orbit is entirely flooded. The solution may be
used freely. To get the most complete anesthesia operation should
not be commenced for about fifteen minutes, although there is a
fair anesthesia in a few minutes.

Enucleation with Insertion of a Prosthesis.—To give motility
to the stump after enucleation, and to prevent sinking of the upper
lid, many surgeons use a prosthesis placed in Tenon's capsule.
Fat and paraffin have not met with general favor. Fat is quickly
absorbed—as a member of the American Medical Association
remarked at the last session, it is "love's labor lost." Paraffin
is apt to be extruded, and when this occurs, the patient is infinitely
frightened and later disgruntled. Glass or gold balls, however,
have maintained their place rather more successfully. Dr. Green-
wood insists that most of the failures have been due to the use of
too small balls, to a careless opening of Tenon's capsule, and faulty
suturing of the muscles. Enucleation with the implantation of a
glass ball is an entirely respectable procedure and may be used
when enucleation is indicated in patients desiring a better cos-
metic effect. It is especially desirable in young children, for
enucleation interferes with the normal development of the orbit
and the glass ball of good size fills the space occupied by the eyeball.

Evisceration.—I believe the best motion and cosmetic effect is
given by evisceration of the eyeball, and yet this operation has
fallen into an unwarranted disrepute. It has been urged against
evisceration that the scleral stump may lead to sympathetic
ophthalmitis. If this is so, it is a sufficient reason for entirely
abandoning the operation, as has been done at Fuchs' clinic. In
opposition is the experience at the Mayo Clinic, where the opera-
tion has been that of choice for many years in uncomplicated
cases. In no case in the last five years has sympathetic oph-
thalmitis developed, as far as can be determined. In cases where

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sympathetic ophthalmitis was considered imminent, the eye has been enucleated, so that if sympathetic ophthalmitis developed in the eviscerated cases, it might fairly have been laid at the door of the scleral stump. Theoretically it is difficult to see how this could occur. While as yet the theories of the propagation of sympathetic inflammation are indecisive, we do know that the seed lesion is situated in the uveal tract, not in the sclera nor the optic nerve. A properly performed evisceration removes every vestige of retina, choroid, ciliary body, lens, and vitreous. What is left is innocuous. Granting that the optic nerve might be the seat of the provocative lesion, nevertheless the nerve is not removed by enucleation, but, on the contrary, becomes tightly adherent to the muscles and conjunctival sac. If a glass ball is used, it is surely capable of irritating the stump of the nerve as much as the normally placed scleral attachment. There is no doubt, however, that bits of retained choroid cause the trouble, as has been proved at least only by histologic examination of the exciting stump. I have sometimes wondered if the laudable desire for an intact globe for laboratory purposes did not have something to do with the prejudice against evisceration. Patients often sacrifice a sympathizing eye rather than have the first eye entirely removed, even if blind, but they will often consent to an evisceration—the fact that not all the eye is to be taken reassuring them, through some curious psychologic process.

An undoubted disadvantage, although not, after all, a very weighty one, is the severe reaction following evisceration. This is greater than after any other method. The second to the fifth days may be very painful to the patient, though rarely requiring morphin. The healing time is considerably longer, as well as the interval before a glass eye can be worn. Further, a general anesthetic is necessary for all except patients of relatively phlegmatic dispositions, although patients are often grateful to have avoided a general anesthetic, even when the pain was considerable. The choice between general and local anesthesia should be left largely to the patient, save in cases where a general anesthetic might involve risk. On the whole, unless sympathetic inflammation is

threatening or enucleation is otherwise indicated, as stated above, evisceration seems to be the operation of choice because of the very good cosmetic result and the simplicity of the operation.

A few points regarding the technic may be mentioned. The opening of the globe may be most easily and painlessly made with a cataract knife, or in default of this, an old scalpel ground down small (Fig. 230). The incision should then be completed with the scissors, following the limbus closely, save at the nasal and temporal

Fig. 230.—Evisceration.   Initial incision.

sides, where the superior and inferior lips meet in a little V, apex away from the cornea, running a few millimeters into the sclera (Fig. 231, a and b). This gives smoothly apposing edges of sclera instead of a double pucker. One or two sutures of silk or small catgut are used to hold the lips together from above down. Too close suturing does not allow the blood to drain easily and will cause pain. Borrowing a point from the operation for hemorrhoids, I cut several radiating slits in the conjunctiva to allow the edema following the operation free drainage. The use of carbolic acid

or Harrington's solution after curetage of the scleral sac is unnecessary and gives rise to a more severe reaction. The scleral sac should be demonstrated clearly before suturing, making sure that every vestige of choroid and ciliary body has been removed, and this is the one indispensable point in evisceration.
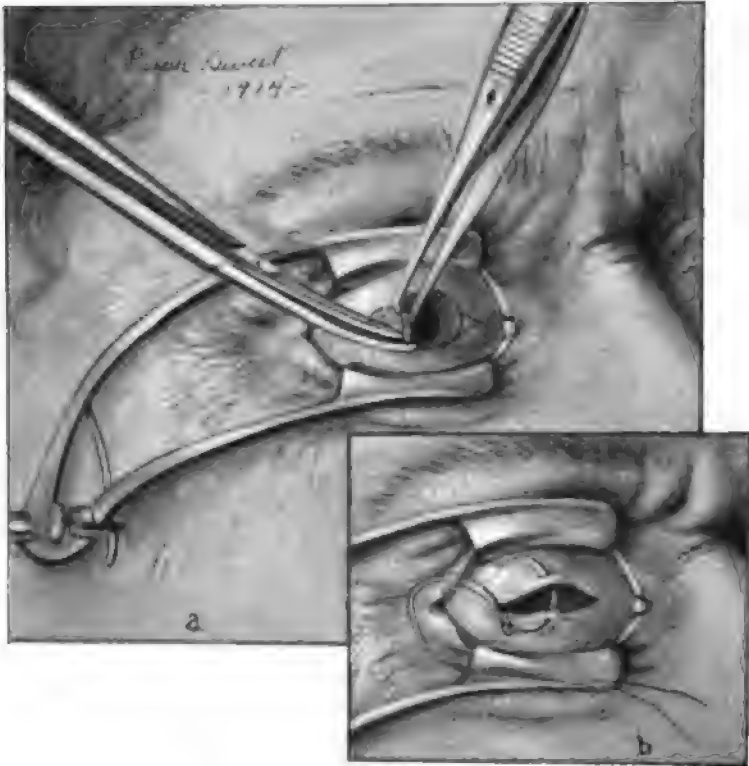
Fig. 231.—a, Evisceration. Excision of cornea. b, Suture.

Evisceration with the Insertion of a Prosthesis into the Scleral Cup.—For the sake of completeness, I may add that, as far as I know, the insertion of a prosthesis into the scleral sac has been entirely abandoned, due to the fact that the foreign body was usually extruded.

Briefly, we may say then that evisceration, from its simplicity

and very superior cosmetic effect, is the method to be preferred save when tumor, infection, pain, or sympathetic ophthalmitis indicates enucleation. If enucleation be performed, a glass ball inserted in Tenon's capsule is a procedure sufficiently reliable to have held its place among good operators and gives a good cosmetic result. Simple enucleation without suture gives an easy, quickly healing stump which requires almost no care afterward and is the operation of choice when these considerations are important and cosmetics are not, as well as under the pathologic conditions just mentioned.

TONSILLECTOMY IN CHILDREN FROM THE STANDPOINT OF THE GENERAL SURGEON *

DONALD C. BALFOUR

The surgeon whose work is not restricted to a special field is frequently called upon to remove tonsils. Unfortunately with the laity, and too often with the surgeon also, there is a tendency to look upon this operation with more or less indifference and with a feeling that it is a comparatively simple one. Undoubtedly, as the operation was carried out formerly, and, to a less extent, at the present time, it could be considered free of any technical difficulty, but this very simplicity was often the indirect cause of an incomplete operation and an unsatisfactory result. Attention has been drawn repeatedly to the fact that many children who supposedly had their tonsils removed have either failed to obtain relief for the symptoms for which they were operated on, or have later in life developed local or constitutional disturbances from hypertrophied stumps of tonsillar tissue.

In spite of considerable uncertainty as to the exact function of the normal tonsil, and of much protest both in the lay and medical press against the so-called "slaughter of the tonsil," it is true that diseased tonsils are often the source of ill health, both in children and in adults. To what extent the tonsil should be held responsible for various forms of arthritis, lesions of the gastro-intestinal tract, infections of the gall-bladder, tuberculosis, exophthalmic goiter, etc., remains to be elucidated by those who are investigating the subject. The work of Rosenow is particularly suggestive and promises important knowledge along this line. Inasmuch as

such strong differences of opinion exist as to the rôle the tonsil plays in various conditions of obscure etiology, one should exercise careful judgment as to the necessity or advisability of tonsillectomy.

Without entering into a detailed discussion of the indications for the removal of the tonsils, it seems logical surgically that if the tonsils are visibly diseased or obstructively enlarged, or if they can reasonably be considered the atrium of infection for some local or constitutional disturbance, both glands should be entirely removed. While tonsillectomy is now rather generally advocated as the operation of choice, yet it is not consistently carried out. For instance, statistics from the New York public schools, where investigation of the condition of the throat following tonsil operations was made, show that in 10 per cent. of the children there had been mutilations of the soft parts surrounding the tonsil; of those operated on without general anesthesia, 90 per cent. of the operations were badly done, and of those operated on under general anesthesia, 25 per cent. of the operations were badly done.

Assuming in a given case that the advisability of tonsillectomy is apparent, what method should the general surgeon adopt if he is to do a complete and effective operation? Numberless instruments are offered to make the operation easy. Practically all these are based on the guillotine principle and are modifications of it. It is significant that those surgeons of the greatest experience with these instruments admit a varying percentage of cases in which the instrument could not be used or failed to remove the entire tonsil, necessitating resort to dissection to complete the operation. It is, therefore, true that dissection, properly performed, will accomplish tonsillectomy in 100 per cent. of cases, while any of the modified guillotine operations will prove inefficient in a varying percentage of cases.

Dissection cannot be advocated as a uniformly easy method, for tonsillectomy varies in difficulty just as do most surgical procedures. In difficult cases the operation, if properly carried out, that is, without damaging trauma to the faucial pillars or other surrounding soft parts, and without risk of hemorrhage, infection,

etc., cannot be classed as a "minor" one. Further, statistics show that the operation is not devoid of these serious complications or even of mortality. It thus seems incumbent to select some method which is safe as well as adequate.

The importance of an anesthetic administered by one who is accustomed to inducing the particular anesthesia which is desired in these cases is quite evident. Failure in this regard is often the cause not only of unsatisfactory operations, but of other disastrous consequences. The child must be thoroughly asleep, so that unabolished reflexes will not interfere with the dissection; but the depth of anesthesia should not exceed a point which is just commensurate with the average length of time necessary for the removal of the tonsils. It is not objectionable for the child to show signs of returning consciousness when the first tonsil has been removed. More ether can then be administered, while a little pressure with the gauze-covered finger may be advantageously applied to the recess from which the tonsil has been removed. The ideal anesthesia is one which is sufficient for the operation, yet light enough so that the patient is already returning to consciousness by the time the operation is completed.

Dissection offers the least liability to primary or secondary bleeding. In this regard lies one of the most important advantages which the dissection method possesses. In only one case has hemorrhage been seen in the cases operated by this method which caused any concern, and that was readily controlled by suture. The absence of bleeding is due mainly to the fact that removal of the entire tonsil permits the tonsillar vessels to retract into the muscular wall of the pharynx. The slight hemorrhage differs strikingly from that which often occurs from the tonsillar stump following tonsillotomy.

As to the special technic of the operation, there is much less to be said than to be acquired. A modification of the Waugh method was introduced into the Mayo Clinic some four or five years ago by Beckman. It has proved satisfactory in the 1654 cases which were operated on under anesthesia from January 1, 1909, to December 1, 1914.

Good anesthesia is the first essential. The position of the child should conform to the individual preference of the operator. We prefer the child lying with the head free over the head of the table, which should be slightly lowered. The child's head is supported by the hands of an assistant, who stands at one side of the table. On the opposite side is an assistant who assists by

Fig. 232.—Finger behind posterior pillar elevating tonsil.

traction of the tongue, sponging, etc., while the operator stands at the head of the child, between the two assistants.

A Whitehead mouth-gag without the tongue-depressor is fixed in place. The operator's index-finger is introduced behind the posterior pillar of the tonsil, and by firm upward traction of the tonsil the anterior pillar is put on the stretch. With blunt dissecting scissors or tissue forceps the pillar is then well freed

from the anterior surface of the tonsil, care being taken not to break through the capsule of the tonsil. This enables the operator, by means of the supporting finger behind, to force the tonsil well forward and to engage the tonsil securely with a tenaculum (Fig. 232). Ordinary uterine tenacula, although they have a tendency to tear into a soft, friable tonsil, when carefully manipulated are very satisfactory for this purpose.

Fig. 233.—Anterior pillar separated and pushed back from capsule of tonsil.

Having a firm hold on the tonsil, it is turned over, so to speak, to expose the posterior pillar, and this is freed usually by blunt dissection (Fig. 233). The superior pole is now enucleated from the superior tonsillar fossa, and, in the majority of cases, the tonsil may then be rolled out of its bed without any more than blunt dissection. In very adherent glands one proceeds slowly, first getting the pillars well separated, followed by blunt dissection,

where possible, or by careful slipping with the dissecting scissors until the tonsil is entirely freed from the pharyngeal wall.

This method enables the operator actually to see what he is
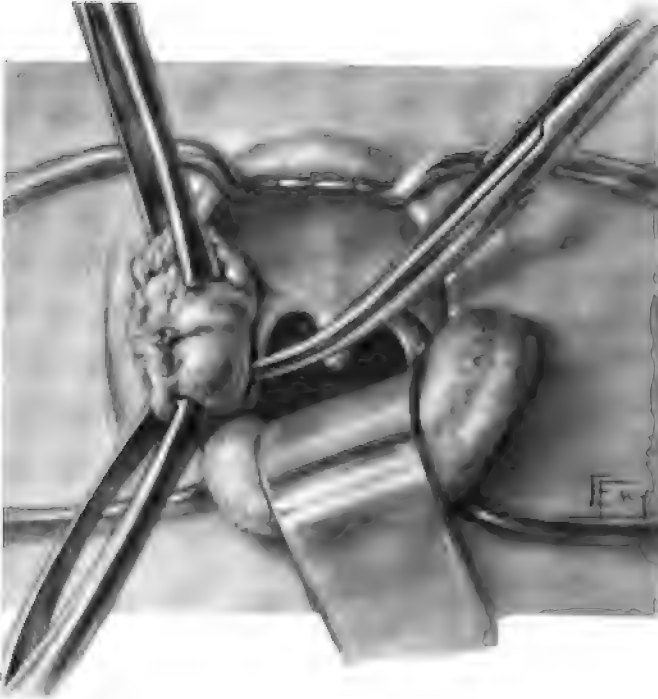
Fig. 234.—Tonsil turned and dissection completed by separating posterior pillar.

doing, and, for this reason particularly, possesses distinct advantages as a precise and safe operation in the hands of the competent general surgeon who has acquired the technic and who appreciates the fact that the operation demands skill, care, and experience.

TREATMENT BY CAUTERY OF GASTRIC ULCER *

DONALD C. BALFOUR

Whatever differences of opinion may exist as to the treatment of gastric ulcer, it is at least accepted as logical that the ideal procedure in our present conception of "surgical treatment" should be the removal of the ulcer. In a given case of gastric ulcer in any situation, except perhaps at the pylorus, the first problems to be settled are whether the ulcer can be excised with safety, what method shall be employed, and whether the excision should be followed by a gastro-enterostomy.

It is not my purpose to discuss at this time the merits of the various principles advanced in the treatment of gastric ulcer, but rather to draw attention to a method which I believe will find a place in the treatment of at least a certain percentage of these cases. In describing this procedure, however, it may be advisable to refer to some of the more serious problems to be met with in the excision of a gastric ulcer.

It may be safely stated that, as a general rule, the chief difficulty is not the removal of the ulcer except when located high on the lesser curvature, but rather the satisfactory closure of the opening thus made. The treatment of gastric ulcer by excision and suture, with or without gastro-enterostomy, may be a formidable operation even in the hands of experienced surgeons, and one which entails considerable risk to the patient.

The most immediate postoperative dangers are those of hemorrhage and impaired gastric motility incident to interference with

the nerve supply in extensive excisions along the lesser curvature. Later complications are usually due to the deformity resulting from contracture at the point of closure.

Hemorrhage occurring late, that is, after the seventh or eighth day, is occasionally of serious consequence. The condition is

Fig. 235.—Ulcer on anterior wall with gastrohepatic omentum dissected from lesser curvature.

somewhat deceptive in that the bleeding is not profuse, but persistent, and may. result fatally, as has recently occurred in our clinic, in which case a secondary gastro-enterostomy and transfusion of blood failed to prevent a fatal issue. The autopsy in

this case showed that the mucous membrane had separated and left a large denuded area from which the bleeding had taken place. Such a complication at such a time is probably dependent upon the fact that after the excision of the ulcer there is a marked tendency of the mucosa to retract, and the tension required to ap-
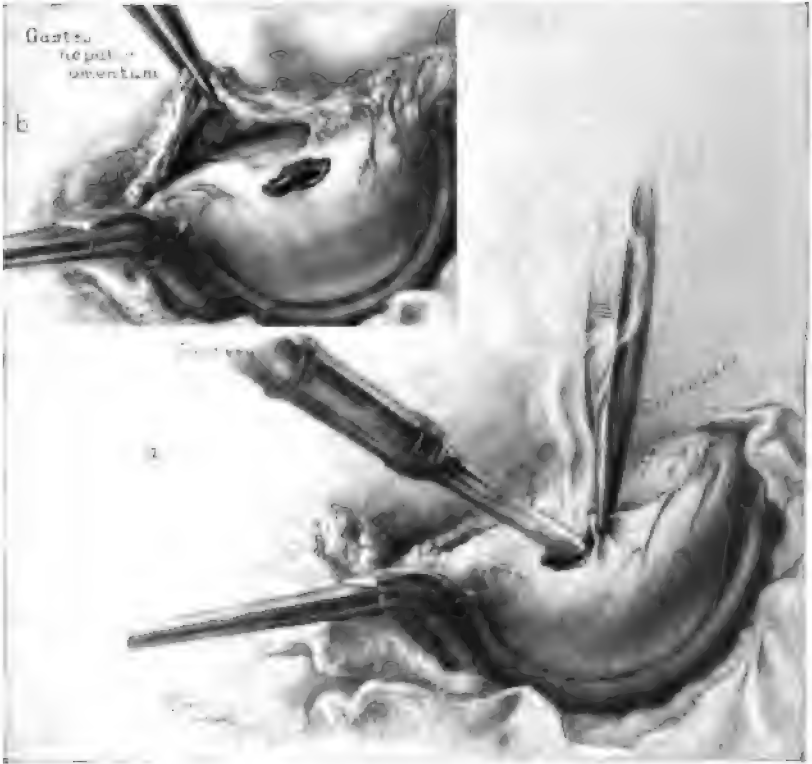
Fig. 236.—a, Burning out ulcer; b, ulcer burned completely through.

proximate it may predispose the sutures to give way during the second week.

In observing the seriousness of these complications, particularly of late hemorrhage, it occurred to the writer that some method might be devised whereby the ulcer could be destroyed in such a manner as to obviate any possibility of hemorrhage, either early

or late, without removing an appreciable amount of healthy gastric wall. That this could be accomplished by the actual cautery seemed obvious. The cautery is one of the most satisfactory methods of dealing with many superficial ulcerations, early epithelioma, certain forms of carcinoma (cervical, buccal, etc.), by virtue not only of its destruction of tissue but also its inhibition of hemorrhage. The application of the principle described here-
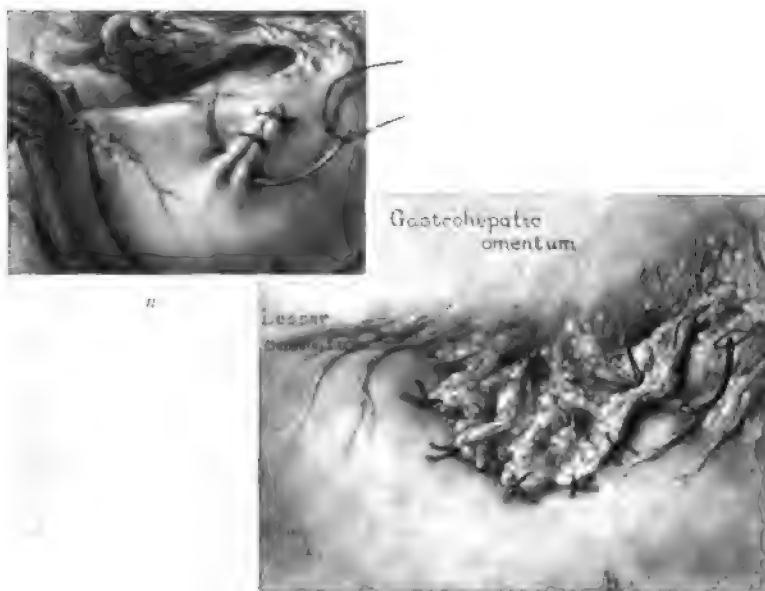
Fig. 237.—*a*, First row of sutures closing opening from which ulcer has been excised; *b*, ulcer area covered by gastrohepatic omentum.

with was, therefore, suggested, and while it has been used in the Mayo Clinic in a sufficient number of cases to warrant reporting, we are not as yet in position to state how the size, character, and situation of the ulcer will affect the limitations of the method. The following technic has been employed in the cases thus far operated on by this method:

The portion of the gastrohepatic omentum in the region of the ulcer is carefully dissected free from the lesser curvature (Fig. 235).

The ulcer is carefully palpated, and with a Paquelin cautery maintained at a dull heat the point is slowly carried through the ulcer until an artificial perforation is produced. The moderate burning is continued until the actual area of the ulcer is entirely destroyed (Fig. 236, *a*). The resultant perforation is shown in Fig. 236, *b*. The opening is then closed by interrupted sutures of chromicized catgut reënforced by mattress sutures of silk (Fig. 237, *a*). The reflected gastrohepatic omentum is then replaced over the site of the ulcer and fixed by superficial interrupted sutures of fine silk (Fig. 237, *b*).

In the application of this method the following facts are apparent:

1. The ulcer is destroyed, and with it any early malignancy which may exist.

2. There is little sacrifice of sound gastric tissue, and secondary contraction is, therefore, minimized.

3. Hemorrhage, early or late, is with practical certainty prevented.

4. Its simplicity, speed of accomplishment, and safety.

THE TECHNIC OF CHOLECYSTECTOMY *

EDWARD STARR JUDD

The two great dangers in removing gall-bladders are hemorrhage from the cystic artery and injury to the common bile-duct. Hemorrhage may occur at the time of operation, or may come later from slipping of a ligature. Injury to the duct may occur through clamping off the cystic duct too closely, or, more commonly, through efforts to stop bleeding from a cystic artery which has slipped while being ligated.

Cholecystectomy is best accomplished from below upward. The important reasons for this are that the dissection from below upward is easier, and the circulation is controlled at the start. It is essential to know the condition of the common duct, head of the pancreas, and lymphatic glands before removing the gall-bladder, and, in the dissection that exposes these, the cystic duct is freed.

STEP I.—The abdominal incision, instead of being made over the normal location of the gall-bladder, is made high and close to the midline, usually extending to the ensiform. Through this high incision, in most cases, much of the right lobe of the liver can be rolled out by using the gall-bladder as a tractor. If the liver is adherent to the parietal peritoneum, the adhesions should be freed before proceeding further, as the operation is much simpler if the liver can be displaced.

STEP II.—An assistant gently tracts on the pair of forceps which is caught to the fundus of the gall-bladder. The neck of the gall-bladder is then caught with a second pair of forceps, and

this part of the gall-bladder and the cystic duct are pulled away from the surface of the liver.   Considerable fat and edematous tissue may be encountered in this region, especially if there is an empyema of the gall-bladder, but this fatty tissue can be cleared
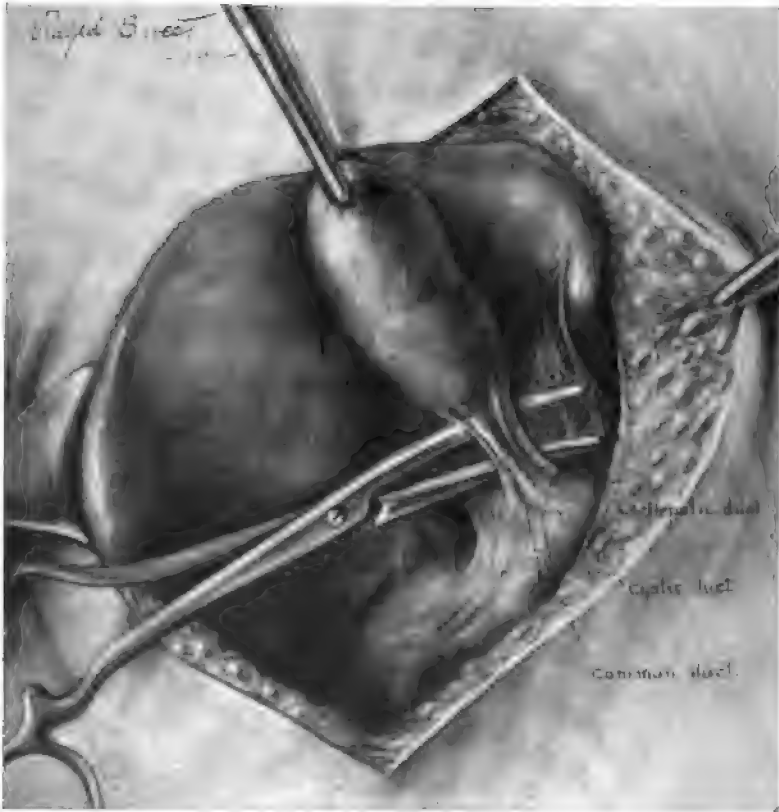
Fig. 238 —High abdomina incision extending to ensiform if necessary.   Grasping gall-bladder undus in soft clamps, the liver is rolled out in the usual way.   An additional clamp may be put on the gall-bladder near the cystic duct to tract the gall-bladder and cystic duct away from the liver so that by blunt dissection the cystic duct and artery are separated from the surrounding tissue.

away from the duct by a blunt dissection.   Tracing down the cystic duct as a guide, the common duct is usually readily exposed by this traction on the neck of the gall-bladder.   The neck of the gall-bladder and the lowest part of the body of the gall-bladder

frequently lie alongside the cystic duct, so that when this is dissected out and pulled up, the cystic duct is easily separated from the surface of the liver (Figs. 238 and 239).

Fig. 239.—Isolated cystic duct with vessels is clamped away from common duct.

STEP III.—The cystic duct and cystic artery are kept together. After these are completely freed from the surrounding tissues for the distance of a half-inch to an inch, they are caught together in two clamps and divided between the clamps. It is this particular step in the technic that I wish to emphasize. If the dissection at

this point is carried out as described, the cystic artery is definitely
ligated without tension, and the common duct cannot be injured
because the grasp of the forceps includes nothing but the cystic
duct and artery.

Fig. 240.—Cystic duct severed between clamps. Gall-bladder turned out. One clamp under the cut-off end of the gall-bladder catches any little vessels not included in the clamp on the cystic duct.

STEP IV.—After dividing the duct and vessels between clamps,
the end of the gall-bladder just cut off from the duct is pulled
upward with a little tension, thus exposing the peritoneal folds
and the communicating vessels at this point.   These vessels are

caught, and the gall-bladder is dissected from its attachments to the liver (Fig. 240).

Fig. 241.—Gall-bladder dissected out in the usual way and fissure in the liver sutured.

STEP V.—The stump of the cystic duct and the cystic artery are now ligated with one ligature of ordinary catgut. It will be

noted that this is done before the gall-bladder has been entirely removed. This attached gall-bladder makes an ideal retractor, and traction on it gives good exposure for the ligation of the duct

Fig. 242.—Drain down to cystic duct.

and artery. As soon as these structures are ligated, the ligature is cut and they are allowed to drop back free from the liver.

STEP VI.—A suture is now started through the cut edges of the peritoneal folds, from which the neck of the gall-bladder has been removed. This is continued upward to the edge of the liver

and is made to cover as well as possible the raw surface left in the liver.   The gall-bladder is removed a little at a time and then a few stitches are applied.   If there is oozing from the surface of the liver, one or two extra stitches may be necessary, though usually a little pressure and relaxation of tension will control it (Fig. 241).

STEP VII.—A small cigaret drain is placed down to the cystic duct and brought out so it will lie in the fissure from which the gall-bladder was removed (Fig. 242).

This technic does not vary in many essentials from that often described.   The important step in the operation is the complete freeing of the cystic duct before it is cut.   Sometimes this is difficult, though it can be done in practically every case.

THE ADVANTAGES OF THE DOUBLE RESECTION IN CERTAIN TYPES OF GOITER*

DONALD C. BALFOUR

The surgery of the non-toxic and non-malignant enlarged thyroid at the present time is attended by practically no mortality. That this fact is known to the laity is evidenced by the increasing frequency of operations on the thyroid by surgeons who are attaining good results, both immediate and ultimate. Realizing, then, that the development of the operative treatment of the thyroid has made safe, in so far as life is concerned, the removal of the so-called simple goiter, further advancement must be made in refinement of technic, in lessening the possibilities of complications, in improving the end-results, and in obviating, as much as possible, recurrence of the condition.

Patients with thyroid enlargement without any evidence of toxemia attributable to the goiter usually desire its removal only for mechanical and cosmetic reasons—that is, pressure and deformity. It is in this group that not only is safety imperative, but also an operation which will offer the patient the greatest probability of permanent relief. With this in mind, I wish to describe a type of operation which, while not original in this clinic, —it being but a modification of the Mikulicz resection,—is being used more and more frequently and with most satisfactory results. The operation is performed as follows:

The usual low-collar incision is made, the external jugular vein marking the limits of the incision laterally. The subcutaneous tissue and platysma are then reflected, the upper flap as high as

the thyroid cartilage, the lower flap to the sternal notch. The vertical muscles, sternohyoid and sternothyroid of one side, are then separated from those of the opposite side by dividing in the midline, from the thyroid cartilage to just above the sternal notch. The thin, peritoneum-like fibrous covering of the gland will then be exposed, and this should be freed over the front of both lobes. The finger is then inserted under this capsule and the entire gland carefully explored to determine the size of the lobes, the relations of the trachea, and the presence of any substernal, retrotracheal, or other isolated portion of gland.

It is now possible to decide upon what should be the further operative procedure. If the exploration reveals a single encapsulated adenoma or cyst in one lobe, with an apparently normal lobe on the opposite side, extirpation of the involved lobe or enucleation of the tumor with division of the isthmus is usually sufficient. If, however, as is so much more frequently found, both lobes are involved in the same process, that is, a diffuse colloid condition, or multiple adenomas of various sizes, we believe the removal of the diseased portion of each lobe is the operation of choice. As a preliminary step, it is often possible to dislocate both lobes from their positions by careful finger-manipulation, after freeing any lateral or accessory veins. In this manner the entire gland in many cases can be tracted to a situation as shown in Fig. 243.

It is immediately obvious, in a large percentage of cases, that removal of the larger lobe will be inefficient in relieving both pressure and deformity, and offers considerable possibility of recurrence of the trouble not only by later enlargement of the remaining lobe, but also because of the retraction beyond even the natural contour of the normal neck which may take place on the side from which the lobe has been removed. A double resection, therefore, in this group of cases seems to be the ideal procedure, and is being more and more frequently employed by us. During 1913, of 1569 operations on patients with various types of goiters, 783 were of the non-toxic or non-exophthalmic type, 583 of which were for so-called multiple or diffuse colloid adenomas. In this latter group of patients, 295, or 55 per cent., were operated on by the double resection method, 116 (21.7 per cent.) had an extirpation of one lobe and isthmus, 122 (23 per cent.) had extirpation of one lobe, isthmus, and part of the other lobe.

Both lobes are dislocated if possible. In doing this completely one often finds that one or both lobes have a tendency to become

flattened out and extend behind the trachea, so that this structure is frequently entirely surrounded by the thyroid tissue.   By care-
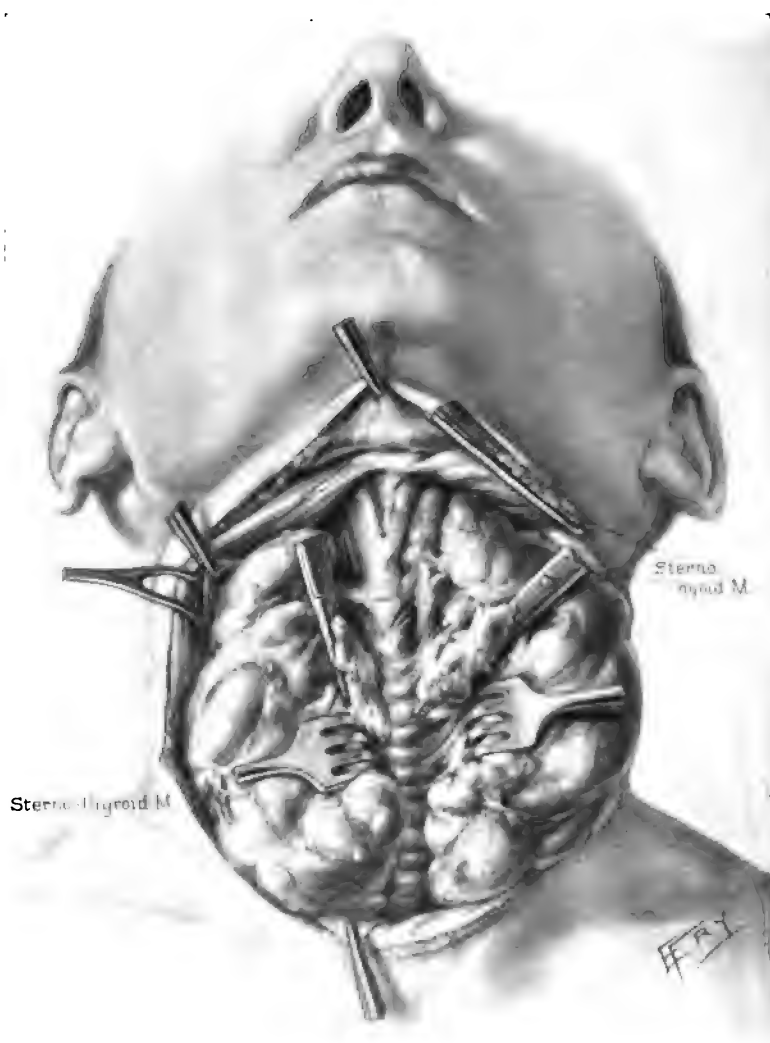
Fig. 243.—Both lobes have been freed from their accessory veins and the isthmus divided between forceps

ful traction the entire lobe of each side can be exposed, and by
inspection it can be determined what portion of each should be
removed in order to obtain a good end-result.

The first step in the actual removal consists of a division of the
isthmus.   This in some cases entails considerable oozing, especially
when the structure is of any thickness, but in the majority of cases,
if the operation is done with care and an effort made to find the
narrowest part, little difficulty will be encountered.   In some cases
the isthmus can be lifted from the trachea, two forceps clamped
entirely across, and complete division made between these.   The
segment of isthmus of one side is then freed from any further at-
tachment to the trachea, and by steady traction and careful dis-
section the lobe on that side is freed from the trachea anteriorly
and laterally sufficiently to relieve all pressure and to permit of
satisfactory suturing after the resection.   The other half of isthmus
and the opposite lobe are then freed in the same way, disclosing
the arrangement of the parts shown in Fig. 244.

Either lobe is now resected.   The following has been found a
convenient and safe method.   A series of Ochsner forceps are
applied somewhat as follows: One at the superior pole, as a rule
about an inch from the upper extremity, one at the inferior pole,
three or four laterally, placed on the larger vessels in the capsule
and two or three on the tracheal side.   These forceps appropriately
placed serve the joint purpose of marking the limitations of the
resection and of enabling one to control hemorrhage by traction on
them along with support of the lobe from behind with the finger.
The lobe is then encircled with an incision through the capsule
just above the forceps.   The resection is then made by "wedging"
out the interior of the gland.   In practically all multiple adenomas
the colloid masses will separate easily from the healthy gland by
finger enucleation.   In the diffuse colloid glands without tumors
the proper portion to resect is readily determined.   Having com-
pleted this, there will be remaining the superior pole, the entire
posterior capsule with a layer of gland tissue and oftentimes the
inferior pole, so that the portion of the gland most closely approach-
ing the normal has been retained.   This cup-shaped structure is
now rebuilt into a compact strip of gland tissue by suture.   We
have found the following method of suturing very satisfactory:
Starting at either pole, a continuous mattress suture of plain cat-
gut from outer to inner capsule is inserted behind the line of for-
ceps originally placed on the capsule and continued to the other
extremity of the lobe.   This controls practically all the bleeding

and obliterates the cavity in the center of the lobe. The same suture, returning in an opposite direction, by a locking or button-hole stitch, catches the edge of the capsule and rolls the two edges together into some semblance of a normal lobe. This recon-structed lobe is then allowed to drop back into the space formerly occupied by the enlarged gland. The opposite side is treated in the same way, resecting as much as seems necessary.

The proper amount of thyroid to be left cannot be stated in actual figures. In no case in which this method of resection has been used has there been any evidence of too much thyroid having been removed.

The difficulties of this type of operation become less with in-creasing experience, and I believe are more than compensated for by the distinct advantages obtained. In the first place, the opera-tion is eminently safe in all respects. Control of hemorrhage is more certain, if possible, by suture than by ligature. Danger of injury to the recurrent laryngeal nerve is greatly minimized and can hardly occur if the operation is properly performed. Free dissection of the gland from the trachea is permissible, and gives an opportunity for much easier and efficient control of bleeding by suturing from internal to external capsule. The fact that the superior and inferior poles and the entire posterior part of capsule are retained precludes any possibility of removal, injury, or inter-ference with the circulation of the parathyroids. This operation is of particular value in treating large goiters, which, by long-con-tinued pressure on the trachea, have caused a softening of the rings. In these cases a temporary tracheal collapse sometimes occurs when the pressure on one side is relieved and the surgeon is in an awkward predicament under such circumstances, if the trachea is not quickly available. By this method the exposure of the trachea as a first step gives immediate and continuous con-trol of the situation.

The benefits to the patient from this type of operation are well defined. All sense of pressure is relieved, and the neck is made quite symmetric, which cannot be said of some of the cases in which an entire lobe has been removed and the opposite lobe left untouched. After such an operation one can assure the pa-

Fig. 244.—a (left lobe), Shows controlling forceps placed and resection of lobe begun. Right lobe resected, with running mattress suture being placed; b, shows the relationship of the built-up remnants of the gland.

and obliterates the cavity in the center of the lobe. The same suture, returning in an opposite direction, by a locking or button-hole stitch, catches the edge of the capsule and rolls the two edges together into some semblance of a normal lobe. This recon-structed lobe is then allowed to drop back into the space formerly occupied by the enlarged gland. The opposite side is treated in the same way, resecting as much as seems necessary.

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tient that there will be much less liability of recurrence of the goiter than with any other type of operation.

The cases to which this operation is applicable are in general the diffuse colloid adenomas. It is not necessary, of course, in the single cystic thyroid, where the trouble is due to an isolated tumor in the gland. It has a very limited field in the exophthalmic group where symmetry is a secondary consideration and the patient is operated on for relief of symptoms only.

THE PREPARATION OF DRY BONY AREAS FOR SKIN-GRAFTING *

CHARLES H. MAYO

The method herewith described for hastening the healing of de-
nuded surfaces of bone is so seldom used as to warrant a brief
description. The extreme slowness of healing of such large ex-
posed areas of bone is a source of great discomfort as well as pro-
longed disability to the patient. Such areas may be located on
the tibia or the maxilla, but are usually on the skull, most com-
monly occasioned by denudation from traumatic scalping. Cases
have been reported that were from one to two years in healing.
They may have been occasioned by burns, by infections,—especially
with the pneumococcus,—or by the removal of large malignant
periosteal growths. In the latter case, the periosteum being
involved in the growth, the safest surgical procedure is radical
excision of the scalp with the tumor and scraping of the periosteum
from the bone. Malignant disease of the periosteum has a great
tendency to recur, and is best treated by thorough application of
the actual cautery to the bony surface. Occasionally such a
wound may be covered by skin-grafting or by sliding over it
adjacent tissue. Such areas are often too large and unfavorably
located to cover with pedicled flaps, and in malignancy it is not
always advisable to do so, nor to attempt immediate skin-grafting,
as thereby one may cover areas containing undestroyed malig-
nant cells. If the wound is left open, should disease recur, it may
be recognized early and subjected to treatment. The margins of
the wound throw out granulation tissue, which soon starts a red

line of osteoporosis at the margin of the exposed bone. After many months the hard outer layer either shells off in a flake or comes away in particles as the granulations spread over the wound after penetrating the outer bony layer. The process, however, may require several months before a suitable area for skin-grafting is secured.

Fig. 245.—Drilling surface to diploë.

To avoid this long delay, for many years I have practised a method which has reduced to a short period a process which formerly took months. The principle involved is not new, but the simplicity of the technic readily adapts it to frequent use. By means of a small drill the entire dry area of bone is perforated like a sieve, or cribriform plate, all over its surface (Fig. 245). These perforations are about ¼ inch apart and penetrate to the diploë

of the skull or to the blood-supply of the bone involved, so that each perforation shows a slight hemorrhage. Through these perforations granulations are rapidly thrown out and soon merge

Fig. 246.—Granulations appearing through outer plate for blood-supply to graft.
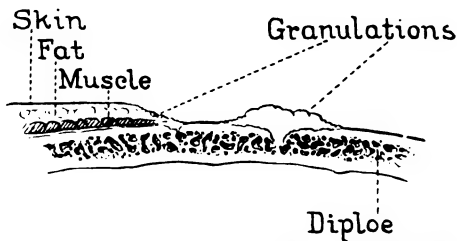
Fig. 247.—Transverse section showing granulations and opening into diploë.

on the surface, allowing an abundant blood-supply for the skin-grafts (Fig. 246).

Since infection of the diploë or vascular area of the bone may occur, such a wound must receive excellent care, at least until protective granulations appear. During a number of years past

'14—37

several cases have been thus treated. These have included large areas of the skull remaining after the excision of carcinoma, sarcoma, or infections with pneumococci. The speedy healing of the wound has been very gratifying.

Occasionally, also, recurring ulcer of the leg in elderly people involves the bone. The usual history is that when young they had a prolonged osteomyelitis with extensive destruction of both bone and soft tissues. The scar of the skin is solidly attached to the bone, which early in life furnishes nutrition to it, but as time passes the bone becomes of ivory hardness and occasions indolent ulcers, due to malnutrition, which recur from time to time. While some cases may be readily covered by sliding adjacent tissue over the areas, it is a simple process to drill a few openings into the bone until it bleeds freely. The resulting granulation tissue with its new vessels then furnishes nutrition for the denuded bone.

ANESTHESIA IN SURGICAL RESEARCH

A Simple, Economical and Efficient Apparatus for Ordinary Routine Work *

BERNARD FRANCIS MCGRATH

The method herewith depicted and described contains nothing which is new in principle. It is presented for what it is worth, as a well-tested, efficient, and comparatively inexpensive routine procedure. Anesthesia is induced by means of a cabinet and continued with the apparatus shown in the figures. A rubber tracheal tube is attached to the horizontal limb of a three-way metal tube (Fig. 248). The latter contains within its lower limb an inlet valve, and an outlet valve within its upper limb. The former valve opens with inspiration to admit ether and closes with expiration; the latter closes with inspiration to exclude air and opens with expiration. The lower limb is inclosed in rubber tubing and inserted into the neck of a can of ether. A small opening is made in the top of the latter, allowing a current through the ether vapor. In a side of the upright of the three-way tube is an opening for the admission of extra air. The amount of air is regulated by a perforated cuff. The three-way tube with its usual attachments may be sterilized. Some of the various combinations which may be effectively employed with the apparatus are shown in Figs. 249, 250, and 251.

Application.—Under deep anesthesia the jaws are separated, held apart with loops of strong tape, and the tongue is drawn forward with forceps. The laryngeal opening is made visible and easily accessible by means of gentle traction on forceps lightly
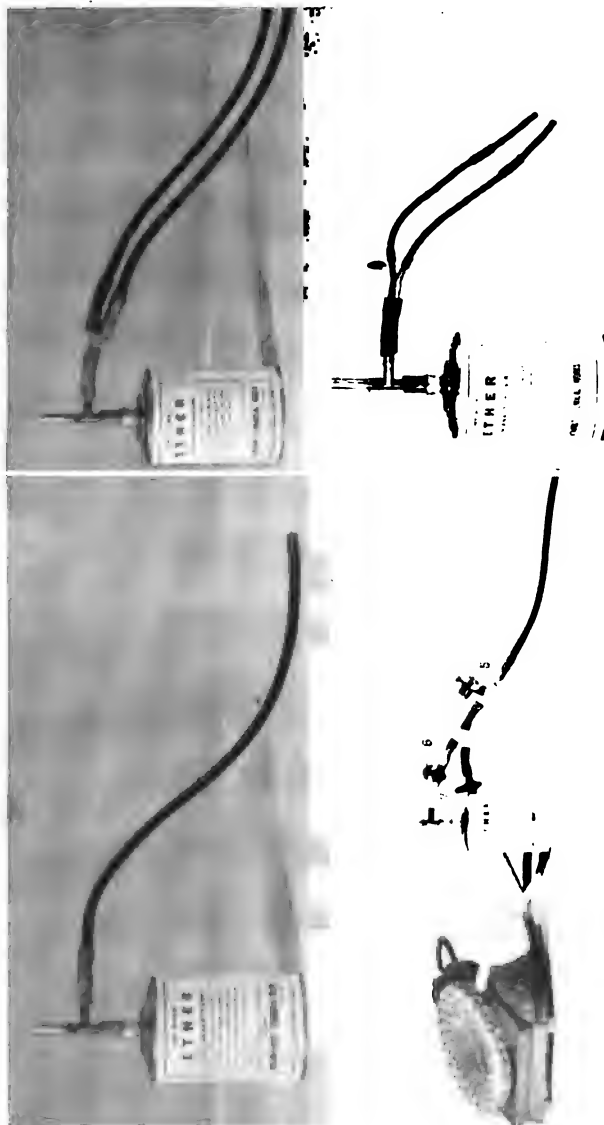
Figs. 248 and 250

Figs. 249 and 251

Fig. 248.—1, location of *inlet* valves; 2, location of *outlet* valves; 3, opening and cuff for regulating extra air; 4, tracheal tube.

Fig. 249.—By removing the *inlet* valve and applying the arrangement shown in this figure, two animals can be anesthetized with one apparatus. This has been successfully employed in 14 cases of transfusion.

Fig. 250.—Foot bellows for insufflation, tube (5) for kymographic record of respirations, and regulating stop-cocks (6 and 7) may be added to apparatus.

Fig. 251.—Intranasal method. The mouth is closed to exclude air as far as possible, and absorbent cotton packed about the tubes in the nose. Commonly used before intratracheal method was adopted. The latter is preferable.

applied to the frenum of the epiglottis. The tip of the tracheal tube is inserted into the opening of the larynx, the left index-finger placed behind as a guide, and the tube now passed into the trachea.

The mouth is held closed with a piece of tape, and, if necessary, a small amount of absorbent cotton is placed in the anterior nares. There is usually sufficient space between two teeth for the tracheal tube. This apparatus has been used by the writer in more than 200 cases. It is practically automatic, requiring but little attention, and, consequently, may be useful in the absence of adequate assistance or where equipment is limited.

VASCULAR SUTURE IN TRANSFUSION

A Simple Device to Facilitate the Work *

BERNARD FRANCIS McGRATH

The therapeutic value of blood transfusion in severe anemia resulting from hemorrhage is generally recognized. Because of the nature of this principal indication, a device for transfusion, in order to be ideal, should be generally available.

Many apparatus have been contributed, but whereas most of them possess some of the essential qualities, none comprehends all.

The methods of transfusion are the *indirect* and the *direct*. In recent times the indirect method has been revived and various devices for its execution have been advanced. The advantages obtained by this method, assuming the employment of the most efficient of these devices, are sureness in transmitting the blood, indication of the amount of blood transmitted, and comparative ease of execution. Many successes have been reported from the use of the indirect method, but, despite this fact, it has strong opponents among physicians of extensive experience. Viewed from the physiologic point of view, the burden of proof still appears to rest on the shoulders of its advocates. The appliances employed in the direct method may be divided into two general groups, namely, one in which a tube is interposed between the vessel of the donor and that of the recipient; the other, in which the intima of the donor's vessel is applied to the intima of the recipient's vessel. In the strict physiologic sense, the latter of these two groups is the true direct method, since the blood comes in contact

with no foreign substance, and, consequently, is transmitted in its normal condition.

The various apparatus of the present day for aspiration-injection, together with connecting tubes, are modifications of conceptions which date far back in the history of the subject; while all cannulas for applying intima to intima are based on Crile's conception. I have already advanced a device for the indirect method. This is a modification of the Aveling apparatus, and consists of a rubber bulb drawn out into two cannula tips.
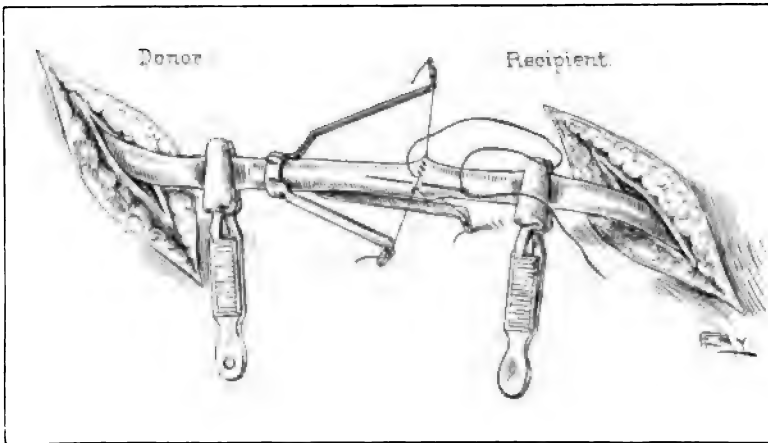
Fig. 252.—Instrument for vascular suture in transfusion as used in anastomosing the vessels. Particularly in transfusion, strong silk may be employed for the stays, the suture being made with the usual fine material for this purpose. Human hair is a very good substitute for the latter in case of emergency.

This has been effective in experimentation. To avoid the possible results of retained clots, a new apparatus should be used in each transfusion. Considering the work, the cost would be negligible. Features in its favor are sureness in transmitting the blood, indication of the amount of blood transmitted, and slight demand for experience. Against it are all the arguments which prevail against the indirect method.

For the direct method I have presented a forceps-cannula. This consists of two very short cannulas which are applied to one another by means of ordinary forceps, made suitably small and

refined for the work. The principle of *cuffing* the vessels, as employed in the Soresi instrument, was adopted. Qualities in its favor are sureness in transmitting the blood, transmitting the blood in its normal condition, and comparative ease of application. Against it may be stated that it is not applicable to very small vessels, and that in case a knowledge of the amount of blood transmitted is desired, it can be acquired at present only by a calculation based on certain factors and indicated by the increase of the recipient's hemoglobin. According to my experience, however, the occasion must be rare in which a vein-to-vein transfusion cannot be accomplished with this instrument. If the veins are of small caliber, the ends may be sufficiently dilated with forceps without detriment to the procedure.

Vascular suture for transfusion has been but limitedly adopted. The reasons are obvious. Cases are encountered, however, in which the object is best accomplished by this means, for example, when the diameter of the vessels is small. Because of this possible indication for its application, and also for the utility of vascular suture in other fields of surgery, any contribution which aims to simplify its technic has a reason for its existence.

The apparatus shown in Fig. 252 is intended to facilitate the procedure of suturing blood-vessels in transfusion or whenever indicated.

Bearing in mind the possible difficulties, the operator should approach every case of transfusion adequately equipped to surmount any obstacle which presents itself.

GENERAL PAPERS

STUDIES IN THE ETIOLOGY OF CANCER

STUDY I.—PRECANCEROUS CONDITIONS*

WILLIAM CARPENTER MacCARTY

The term precancerous has become so indelibly impressed upon our minds in our search for perfect therapeutic results in cancer that it seems necessary to study its real meaning and significance in the light of facts which have been recently determined relative to the histogenesis or development of cancer.

It is a term which has not been completely defined nor accepted by many pathologists to have a definite histologic basis other than the one which the clinician has given to it by considering chronic inflammatory conditions in general precancerous.

In this usage the prefix "pre" has had wide limits in regard to time; it has not been given a definition which means the immediate precancerous stage of cancer.

It is the writer's opinion, from a certain knowledge of literature and some experience with clinicians, that the term is more or less indefinite and needs some explanation; indeed, an explanation which will not only place the term on a histologic basis, but will also indicate certain therapeutic measures which will be of value to physicians, surgeons, and pathologists.

Since the question of cancer is a very large subject, and not only includes many organs, but embraces new-growths of both epithelial and connective-tissue origin, it may be more clearly presented if we consider the question in regard to one organ and confine our observations to cancer which has its origin in epithelial cells.

More correctly speaking, in this consideration the term pre-carcinomatous would be more appropriate. The term should also be confined in this discussion to a condition which immediately precedes cancer.

If one examines a large series of breasts which have been removed for chronic mastitis and for carcinoma, four definite histologic facts are seen:

1. Acini are found which consist of two rows of cells, an outer row and an inner row (Fig. 253).

2. Acini are found in which the inner row has disappeared, and there is a proliferation of the cells of the outer row (Fig. 254).

3. Acini are found in which the inner row of cells has disappeared, the cells of the outer row are hyperplastic, and the line of demarcation between the acini and the stroma is confused and often partially destroyed.

The cells of the outer row are seen in the stroma (Fig. 255).

4. The cells within the acini are often morphologically indistinguishable from the epithelial cells in the stroma (Figs. 254, 260, and 261).

The first two of these conditions have been termed respectively primary and secondary hyperplasia. The last two have been called tertiary or migratory epithelial hyperplasia. The first condition (*a*) is not carcinoma, the second (*b*) may or may not be carcinoma, and the third (*c*) and fourth (Figs. 260 and 261) conditions are certainly carcinoma.

It seems to me that the most immediate precancerous or precarcinomatous condition in these pictures is the secondary epithelial hyperplasia (Figs. 254, 255, 256, 257, 259, 260, 261). The condition is a definite histologic picture, and is one through which carcinoma passes before it can positively be said to be carcinoma.

The three histologic conditions or apparent stages of epithelial hyperplasia which represent a benign condition (primary hyperplasia) and a malignant condition (tertiary or migratory hyperplasia) serve as a basis for definite practical rules for the treatment of mammary epithelial neoplasms.

They apply to any local or diffuse non-encapsulated or encapsulated tumor of the mammary gland with the exception of such rare conditions as sarcoma, endothelioma, myxoma, chondroma, dermoid, teratoma, syphilis, and tuberculosis, and may even apply to these if the behavior of epithelial structures is to be considered as bearing upon the nature of the tumor.

They apply to the more common conditions, such as simple adenoma, simple fibro-adenoma and adenofibroma, or fibroadenoma and chronic mastitis, with or without the presence of cysts.

In general, they apply to all tumors of the breast whose benignancy or malignancy is dependent on the biologic activities of epithelial elements.

This large group comprises the vast majority of pathologic conditions in the breast with which the practitioner and surgeon come in contact, and may be treated according to definite rules:

1. The conditions which are associated with classic clinical signs of carcinoma should be treated radically.

2. The doubtful cases in women near or over thirty-five years of age should have the entire mammary gland removed for immediate examination. If primary or secondary hyperplasia be present, nothing more should be done; if tertiary hyperplasia be present, a radical operation should be performed.

3. In doubtful patients near or under thirty-five years of age a wide sector of the mammary gland, including the pathologic condition, should be removed for examination. If secondary hyperplasia be present, the rest of the mammary gland should be removed, and if tertiary hyperplasia be present, the radical operation should be accomplished.

It may be seen that, in the case of one organ, the precancerous or precarcinomatous condition may be defined as a definite histologic picture, which allows, in fact demands, definite therapeutic procedures.

Since the precarcinomatous condition is a definite histologic entity and has clinical applicability in the breast, it behooves us to determine if similar histologic entities exist in other organs.

In the prostate there are three definite histologic pictures (Figs. 262, 263, 264, 265) which are identical with those which have been found in the breast. However, the anatomic character of this organ does not permit any advice from a therapeutic standpoint, although the presence of secondary hyperplasia should stimulate a guarded prognosis.

The natural pathologic grouping of gastric ulcerations allows somewhat the same consideration which has been advised for the mammary gland.

In the stomach one finds certain facts relating to chronic ulcerations and carcinoma which may be studied in the light of these findings.

Chronic gastric ulcers occur which have all the characteristics of simple chronic gastric ulcer plus the presence in the mucosa of an epithelial hyperplasia the cells of which are indistinguishable morphologically from the cells of early carcinoma. Similar ulcers occur, plus the presence of invasion of the stroma by cells which are indistinguishable from the intraglandular hyperplastic cells. This latter group is certainly carcinoma.

One also finds chronic gastric ulcers in which the borders and bases are definitely involved by carcinoma.

If operative procedure is to be carried out in the treatment of these cases, it may be done according to definite rules. If excised, chronic gastric ulcers show a mucosa which contains differentiated cells (Fig. 266) without the presence of partially differentiated cells (Fig. 267), one should not, with our present knowledge, demand resection. If, however, there is an extensive hyperplasia of partially differentiated cells (Figs. 268 and 269), resection might be indicated when technically possible, if such a resection does not carry with it a greater risk to the patient than does simple wide excision. The clinical significance of what might be called the precancerous epithelial hyperplasia in chronic gastric ulcers may be, therefore, readily seen.

The fact that such a precancerous epithelial hyperplasia does occasionally exist in the mucosa of simple chronic gastric ulcers seems to indicate also at least one clinical consideration, namely,

that it is impossible to determine, by known clinical methods, by gross pathology, or by low-power microscopy, when an ulcer is or is not in the condition of what might be termed secondary hyperplasia or precancerous epithelial hyperplasia.

There is one other organ which has been studied by the writer in the light of histologic proof of the histogenesis of carcinoma.

The skin, when in a condition of chronic inflammation, not infrequently shows cytologic pictures (Figs. 270 and 271) which bear certain resemblance to those which have been found in the breast.

This organ consists of two apparent types of cells, the differentiated or squamous cells and the so-called partially differentiated or basal cells. The latter cells have for their function the renewal of differentiated cells, when the latter have been destroyed, and therefore show evidence of hyperplasia in the presence of chronic destructive processes. They are not only hyperplastic, but present marked irregularities in size and shape, the same characteristics which are possessed by the intra-acinar hyperplastic cells of the outer row in the breast, and which is called secondary or precarcinomatous epithelial hyperplasia.

As in the breast and stomach, these cells are morphologically indistinguishable from the cells which have invaded the stroma in early epithelioma. This fact has a two-fold clinical significance. Since we do not know that such a condition is or is not malignant, one does not dare to do a radical operation. Since we do know that it does bear a cytologic if not a biologic resemblance to epithelioma, the clinician cannot deal with the condition justly unless a wide excision is performed.

It seems to me that these observations allow the following definite conclusions:

1. There is a cytologic basis for the term precarcinoma or pre-epithelioma, and by further study this basis may apply more broadly to the term precancer.

2. The clinician may divide his therapeutic procedures into three types, namely, simple excision, wide excision, and radical operation, with the removal of large amounts of tissue and lymphatic glands, and that these may be based upon definite histo-

logic pictures of a condition which may be called precancerous hyperplasia.

3. The term precancerous may be limited to a cytologic condition which immediately precedes cancer, and should not be utilized to indicate simply a chronic inflammation.

4. Even the cytologic precancerous condition has not been definitely proved always to become cancer.

STUDY II.—THE HISTOGENESIS OF CANCER OF THE STOMACH*

It is generally thought that gastric carcinoma arises from postnatal epithelial rests which are supposed to be present either in the scar-tissue bases or the submucosa of gastric ulcers. Since this idea is theoretic, I take the liberty of presenting briefly some facts relative to the histogenesis of gastric carcinoma and its relation to gastric ulcer.

Simple chronic gastric ulcers have never, in my experience, presented any visible epithelial rests which one could scientifically state were prenatal. Neither have I seen postnatal epithelial rests in the mucosa, submucosa, or ulcer base that were not either composed of atrophic epithelium or real carcinoma, the latter condition being present in the base or submucosa only when there was extensive involvement of the mucosa.

In the simple chronic ulcer (Fig. 273) one frequently finds the glands composed of columnar or cuboid cells, regularly arranged with oval or round nuclei, which are almost always of the same size and are placed near the bases of the cells (Figs. 274 and 275). The cells are sharply demarcated from the stroma, which consists of fibroblasts, differentiated fibroblasts, and some lymphocytes, all of which form a histologic picture distinguishable from the normal gastric mucosa with great difficulty. From this picture to carcinoma there are transitional, apparently intermediary, pictures, the extremes of which are easily distinguishable.

* Read before the Academy of Medicine, Kansas City, Mo., November 20, 1914. Reprinted from Amer. Jour. Med. Sci., 1915, cxlix, 469–476. Copyright, 1915, by Lea and Febiger.

The epithelial cells of the glands in some ulcers lose their cuboid or columnar shape and regularity in size and arrangement (Figs. 276, 277, and 278). They become oval or round, and the nucleoli become larger and more distinct. The exact origin of these cells is at present unknown, since in the gastric gland there are not two distinct rows of cells normally present, as in the breast, prostate, skin, and the accessory epithelial organ of the skin. To my knowledge a germinative layer of cells or a germinative focus of cells has not as yet been satisfactorily demonstrated.

The cells (Figs. 277–282) which are frequently found, however, present a morphologic picture which is indistinguishable from that seen in secondary epithelial hyperplasia in other organs having a germinative layer which is the origin of cancer-cells. Various degrees of intraglandular morphologic changes (Figs. 277–282) are found in the borders until the cells become indistinguishable from cancer-cells (Figs. 279, 283, 284, and 285). When such a condition is found, careful search frequently demonstrates a lack of demarcation between the gland and the stroma, and epithelial cells may be seen in the stroma, the latter condition being accepted by general pathologists to be the criterion of cancer. When cancer is definitely present in the mucosa or other coats of the stomach, the intraglandular cells always present the condition which has been described as secondary hyperplasia in other organs.

From a cytologic standpoint I see no objection to denoting the condition as secondary hyperplasia in the stomach. It is apparent that the histogenesis of cancer in the stomach bears an analogy to that in the breast, prostate, and skin, with the one exception that the germinative stratum or focus has not been demonstrated, a condition which differs from primary epithelial hyperplasia in the organs just mentioned.

Whatever the irritant or irritants are, be they extrinsic or intrinsic, there is an apparent attempt on the part of nature to reproduce the epithelial lining of the glands. In this attempt there is failure completely to differentiate the cells. The coincidental picture of secondary hyperplasia of the cells differs from cancer-cells only in position.

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From these facts one may clearly see that the cancer-cell arises from intraglandular hyperplastic cells of the mucosa, and represents a malignant end-stage of a process of hyperplasia of normal cells.

STUDY III.—THE BIOLOGIC POSITION OF THE CANCER CELL*

The three following failures in my professional experience have been responsible for an extensive investigation of pathologic conditions in the mammary gland: (1) Inability to understand consistently the classifications in the literature of mammary pathologic conditions; (2) inability to understand the structure and function of the "membrana propria," which has played so essential a rôle in differentiating histologically benign from malignant epithelial hyperplasia, and (3) inability to find, in a large amount of normal and pathologic material, such a thing as a prenatal or postnatal epithelial rest which showed any signs of resemblance to early or late carcinoma, and to which any relation to the ordinary neoplasms could be conscientiously attributed. In 1910 I presented three definite diagrammatic and photographic histologic pictures of acini in breasts which were found in conditions known as chronic mastitis and carcinoma.[3]

Acini were frequently seen in which there were two rows of cells—an outer row and an inner row (Figs. 253 and 286). Others were seen in which the inner row was exfoliated, often absent, and the lumina partially or completely filled with the hyperplastic cells of the outer row (Figs. 254, 258, 287, 288, 289). In some acini the inner row of cells was exfoliated or absent, the cells of the outer row were hyperplastic, and the line of demarcation between the acini and the stroma was partially or completely obliterated (Fig. 258). The hyperplastic cells of the outer row were also found in the stroma, thereby producing a picture which

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* Read before the American Association of Pathologists and Bacteriologists, April 10, 1914.   Reprinted from the Pan-American Surgical and Medical Journal, 1915, xx.

is indistinguisable histologically from the one which we know as carcinoma.

The frequency with which these pictures were found naturally stimulated and permitted a hypothesis that carcinoma cells were the direct offspring of cells normally present in the acinus, and were neither derived from the differentiated cells by means of metaplasia nor from prenatal or postnatal cell-rests, according to the hypotheses attributed to Cohnheim and Ribbert. Further investigation of the cells of the acini, with repeated examinations, confirmed the observations and proved that their origin was no longer a hypothesis but a demonstrable fact.

In 1913 the three histologic pictures were described as primary (Figs. 253 and 286), secondary (Figs. 254, 286, 287, 288, and 289), and tertiary or migratory epithelial hyperplasia (Figs. 258, 291, and 292). These terms were utilized to express many histologic pictures in the breast which apparently are parts of a process of epithelial hyperplasia.[4]

On account of the clinical confusion which has existed regarding the malignancy or benignancy of the condition termed secondary hyperplasia, a condition which has been described by at least 13 synonyms, I later described the three pictures from the clinical standpoint as primary, secondary (carcinoma?), and tertiary or migratory hyperplasia (carcinoma), and suggested practical rules for the treatment of such mammary conditions with the hope that some knowledge as to the malignancy of secondary hyperplasia might be obtained, and incision of tumors and unnecessary amputations of the breast might be avoided.[5] The period since the application of these rules has not been long enough, however, to solve this problem.

The fact that the intra-acinic hyperplastic cells of the outer row (Figs. 254, 258, 287, and 289) are often morphologically indistinguishable from the extra-acinic cells of carcinoma (Figs. 258, 291, and 292) has led me to consider the great probability that they are one and the same thing, and that the old criterion for histologic carcinoma, namely, the breaking through of basement-membrane, may be false, and that we may be compelled to con-

sider the condition of secondary hyperplasia on the road to malignancy before invasion of tissue occurs.

In the light of these facts the one question to be answered in this discussion is, What is the biologic position of the cells of the outer row? This may be answered by an investigation of the embryologic development of the breast. If one traces the life-history of mammary epithelium, one begins naturally with the ectoderm of the three-layer stage of embryologic development.[4] This layer of partially differentiated epithelium becomes more highly developed, to form the so-called skin of the embryo. At first it is composed of one layer of low cuboid cells, which, with further development of the embryo, become differentiated to form two or more layers of cells, the outer layer differing from the first layer in being composed of flatter or less cuboid cells, with their long axes parallel with the surface of the body.

With both antenatal and postnatal development, the secondary layers or flattened cells become more differentiated and less like their immediate predecessors, which, in this stage, the embryologists have termed the "stratum germinativum" of the skin, or the germinating layer of the epidermis. The history of the cells of this layer proves that they retain the power of divergence into several structural and functional derivatives. It may be spoken of as a plastic layer, at least in the embryo. This expression of its broad functional capacity is based on its behavior in the development of the appendages of the skin; namely, hair, nails, sweat-glands, sebaceous glands, and the mammary glands.

Histologic specimens which have been taken through embryonic skin and subcutaneous tissue in various portions show developmental activities of the stratum germinativum other than the production of epidermal cells.

The cellular activity of this layer is directed toward the development of hair-follicles and sweat-glands. The downward growth of the germinal cells into the subcutaneous tissue is accompanied by their differentiation into hair- and sweat-producing cells instead of epidermis. The examination of fully developed hair-follicles and sweat-glands shows that there still remains a row

of cells which correspond to the stratum germinativum of the epidermis, and may be considered the stratum germinativum of the hair- and sweat-cells. The epithelium of nails, hair-follicles, sebaceous glands, sweat-glands, and mammary glands possesses its stratum germinativum, from which the differentiated cells of the organs named are reformed.

From this brief statement of embryologic facts which are presented here one may crudely construct a working diagram of the histogenic development and biologic position of the cells which we know as carcinoma cells (Figs. 293 and 294).

The facts relative to the activities of the stratum germinativum of the mammary gland were, at the time of their first observation, sufficient to allow one to predict a similar origin for carcinoma in other organs, especially those in which the stratum germinativum could be demonstrated. During repeated microscopic fresh tissue examinations of the prostate the duplex arrangement of the epithelium in acini was often observed.

A search was made by McGrath and the writer[6] for pictures similar to those which have been described in the breast. Primary (Figs. 295 and 296), secondary (Figs. 297 and 298), and tertiary or migratory (Figs. 265 and 299) hyperplasias were found separately in many slides. The most convincing evidence was, however, the presence of all three apparent stages in the same slides (Fig. 300).

The skin also furnished an excellent example of the presence of the stratum germinativum. In the hope of demonstrating the three stages, or their cytologic equivalent in this organ and its accessory organs, Broders and the writer[7] have examined over 1600 epitheliomas of the skin.

The three pictures of hyperplasia seen in the breast and prostate are not so easily defined in the skin. It may merely be stated that, in some chronic inflammatory conditions of the skin, there is often found an irregular hyperplasia of the cells of the basal layer, or stratum germinativum (Figs. 270 and 271), and that these cells are often morphologically indistinguishable from the cells of typical epithelioma of the skin, especially early epithelioma (Figs. 301 and

302). They apparently bear the same morphologic relation to the cells of epithelioma which the hyperplastic cells of the stratum germinativum of the mammary acinus bear to the cells of carcinoma of the breast. Figs. 301 and 302 show definitely that some of the downgrowths of epithelium of the skin are epitheliomas, and are outgrowths of the dermal stratum germinativum.

In 1914 I published a series of studies on chronic gastric ulcer[7] and its relation to gastric carcinoma in which chronic ulcers of the stomach divided themselves into four groups—i. e., simple chronic ulcers or ulcers in which no histologic evidence of carcinoma was present (Figs. 273, 274, 275, 276, and 277); chronic ulcers which presented all the characteristics of simple chronic ulcer plus the presence, in the borders, of an intraglandular epithelial hyperplasia the cells of which were morphologically indistinguishable from the cells of gastric carcinoma (Figs. 278, 280, 281, and 282): simple gastric ulcer plus an invasion of stroma by a hyperplasia of cells which are similar cells to the intraglandular hyperplastic cells (Figs. 278 and 279), and in which there was an ulceration of the coats of the gastric wall, plus the presence of carcinoma in all the coats, including the ulcer-base and lymphatic glands (Figs. 283, 284, and 285).

In chronic gastric ulcers it is impossible to state that any relation exists between the intraglandular epithelial hyperplasia and the germinative cells of the functionating cells of the glands of the mucosa, because the exact location of the germinative cells of the gastric epithelium is unknown. I may state, however, that the earliest cellular changes I have seen were located in or near the bases of the glands, which is the location of the germinative cells, according to the work of Bizzozero. So far as I have been able to determine from the literature, Bizzozero's statement has not been confirmed. One other point may be stated in reference to the gastric intraglandular hyperplasia, namely, that the hyperplastic cells are apparently cells which are not differentiated to the point of functionating cells of the gastric mucosa, and bear no morphologic resemblance to them.

Certain pictures which have been seen in hair-follicles show

epithelial changes in the position of the normal stratum germinativum of the hair-follicle (Fig. 272), which suggest the secondary hyperplastic condition of the stratum germinativum of the mammary and prostatic acini.

An analysis of the activities of the cells of the stratum germinativum of the mammary and prostatic acini results in the fact that the cells of carcinoma are directly related to and are the direct and immediate descendants of normal germinative cells in these structures. They are not the result of such abnormal conditions as prenatal or postnatal rests which have undergone atypical proliferation.

If analyzed in the light of the biology of the cells comprising these structures, it may be seen that the acini of the breast and prostate consist of two sets of cells, the one set differentiated from the other for the definite purpose of secretion of milk and prostatic secretion, and the other has for its function the reproduction of these differentiated cells. In the presence of chronic destruction of the differentiated cells the germinative cells apparently attempt to reproduce that which has been lost (a natural phenomenon seen in the reproduction of epidermis and nails). In their apparent inability to reproduce the differentiated cells they become hyperplastic and irregular in size and shape, and eventually, in some cases at least, invade the surrounding stroma, lymph-glands, and distant organs by migration.

The histologic pictures of epithelial activities in the skin, stomach, and hair-follicles which are herewith presented are sufficient to suggest a similar development of carcinoma from the stratum or focus germinativum of these organs.

The conclusions to be derived from these facts are:

1. Epithelial hyperplasia in the breast and prostate, and possibly in the skin and the stomach, may be described as primary, secondary, and tertiary or migratory hyperplasia.

2. The membrana propria in the acinus of the breast and prostate is the germinative layer of cells for the secreting cells.

3. The cells of the mammary stratum germinativum are the direct or immediate progenitors of the carcinoma cells.

4. The immediate histologic precarcinomatous stage is the histologic condition described as secondary hyperplasia.

5. It has not been definitely proved that secondary epithelial hyperplasia always shows evidence of developing into cancer.

6. This would seem to indicate a new field of research, i. e., the study of the relation of the differentiated cells of the body to cells which are held in reserve for the purpose of renewing differentiated cells when the latter are destroyed. The germinative cells certainly exist in some organs, and upon further study may be found to exist in other organs. Indeed, the facts which have been demonstrated by a study of the breast and prostate seem to indicate that even the germinative cells of organs of connective-tissue cell origin may likewise play a similar rôle in the histogenesis of sarcoma.

7. The carcinoma cell is biologically neither an embryonic cell nor a metaplastic cell from the functionating parenchyma, but is a direct descendant from cells which have been partially differentiated from the ectoblastic cells for the purpose of reproducing the parenchyma of epithelial organs. By means of some biologic law they fail to reproduce parenchyma, and enter upon an independent migratory existence which is pathologic to the communistic organism.

STUDY IV.—NOTES ON THE REGULARITY AND SIMILARITY OF CANCER-CELLS.*

The studies which have been made of perfectly fresh material of primary, secondary, and tertiary epithelial hyperplasia and their relation to cancer have revealed that microscopic fields of cancer contain epithelial cells possessing certain definite morphologic characteristics. There are cells which are almost perfect spheres, which possess a single spheric nucleus containing one or more spheric or oval nucleoli (Figs. 303 and 304, a, b, c, d, e, f). There are many cells which are ovoids, and likewise contain perfect nuclei and nucleoli (Fig. 304, e and f).

* Read before the Academy of Medicine, Kansas City, November 20, 1914.

In the same fields one also finds spheric or oval planes of cells of different sizes, some without nuclei and nucleoli, some with nuclei and without nucleoli, and some with various sized nuclei and nucleoli (Figs. 303 and 304).

In cancerous tissue which is perfectly fresh, and even in that which is not perfectly fresh, there are some perfect spheric and ovoid cells, these being more common in perfectly fresh tissues, although the dominating cells are really portions of cells or cells in which the outlines of the cell, the nucleus, and nucleolus are distorted and indistinct—qualities which, I believe, are the result of an autolytic process apparently occurring in many cells of neoplasms in the body very soon after the circulation of the tissue is cut off.

The close resemblance of apparently perfect cancer-cells from different organs to the cells of secondary hyperplasia of the same and different organs has suggested the possibility that many of the morphologic irregularities of the cancer-cell which have been described are in reality artifacts which are due to autolysis, and the cutting of various planes of the cells in the process of making thin sections.

Since many cancer-cells are 20 micra in diameter, it is quite probable that sections 5 micra thick cut the same cells several times in serial sections (Figs. 305 and 306). This naturally would also take place in sections of any thickness, but the thinner the section, the fewer will be the number of perfect cells present in the section. In the case of fresh unfixed tissues the sections are usually cut thicker, although 5 micra sections can easily be made with frozen fresh tissue.

The albumin of the cells in unfixed tissue is not coagulated, but retains its translucency and enables one to examine a thicker section, which in my experience has contained many more perfect cells than are found in the fixed sections.

As a result, therefore, of the studies made upon perfectly fresh unfixed tissues, I have been led to believe that the cancer-cell is practically always a perfect cell, with the characteristic component parts of a perfect cell, the variations which have been described

being largely due to cytologic postmortem autolysis, cytologic antemortem disintegration, and the fact that the cells are cut in various planes.

The irregularities mentioned here do not, of course, take into consideration the changes in the cells due to the natural variation in the size of cells of the same kind, and the variation coincident with the stages of mitosis.

It has been further observed that many cancer-cells from the breast, stomach, glandular metastases, and the sigmoid are morphologically indistinguishable from each other and from the cells of secondary epithelial hyperplasia, the last condition being one which the general pathologist does not recognize as carcinoma, and which has not been proved to be carcinoma (Figs. 307, a, b, c, and d).

STUDY V.—NEW FACTS REGARDING CANCER AND THEIR CLINICAL SIGNIFICANCE *

It has been definitely established that the cancer-cell apparently arises in certain organs from cells which are normally present, and which have the definite normal function of replacing the functionating cells of the organ.[4]   They are the immediate offspring of the germinative cells of the parenchyma of these organs.

It has been further established that parenchymal germinative cells of some organs undergo certain morphologic changes in the presence of a chronic irritant or irritants, and that these changes are similar in the breast, prostate, skin, and stomach.   The line of demarcation between the hyperplastic intra-acinic or intraglandular cellular changes and the extra-acinic or extraglandular epithelial cells which are characteristic of carcinoma is not morphologically visible, the only difference being in the location of the cells; intra-acinic or intraglandular hyperplastic cells have been considered to be non-malignant, and extra-acinic and extraglandular hyperplastic epithelial cells to be malignant.

Normal functionating cells, hyperplastic intraglandular and

intra-acinic germinative cells, and extraglandular and extra-acinic hyperplastic cells of carcinoma are frequently seen in the same field of the microscope.[6]

It has been apparent that the most closely related cytologic picture to carcinoma is the intra-acinic or intraglandular hyperplasia, which has been termed secondary epithelial hyperplasia, and that this picture is the histologic condition which should be called the precarcinomatous or precancerous condition.

In 1913 I described the stages of epithelial hyperplasia as primary, secondary, and tertiary, and during the same year presented the practical application of these terms to the mammary gland.[4,5]

Since the terminology which I have adopted as a result of this investigation has proved simple and satisfactory in the case of mammary neoplasms, it has seemed advisable to extend the observations to other organs. The prostate, skin, and stomach have conformed absolutely to this histology and terminology. Such definitely defined terms as primary, secondary, and tertiary epithelial hyperplasia may be utilized in establishing a clearer understanding between the pathologist, clinician, and surgeon in defining benign, doubtful, and malignant epithelial growths. The proposed method, however, involves the undemonstrated danger of spreading a malignant disease by wide excision, both pathologist and surgeon agreeing that incision of neoplasms is a bad and dangerous practice.

In doubtful cases wide excision of pathologic epithelial conditions produces a specimen which may be classified under three distinct and definite headings, each having a definite clinical significance; and that forming the basis of accurately defining the doubtful group of cases, which may be studied with the object of settling the correct operative procedures and the curative effect of operative surgery in its relation to epithelial neoplasms. It may be suggested, therefore, that such a specimen, when removed by wide excision, be classified as primary epithelial hyperplasia, secondary hyperplasia, or tertiary hyperplasia, the first being benign, the second doubtful, and the third malignant. (See Figs.

308-312.) With our present knowledge, the first condition requires only excision, if anything, the second wide excision, and the third complete or radical removal.

In case the pathologist reports secondary hyperplasia, wide excision only is justifiable. It is the second group, which needs careful study because the exact outcome of such a condition can be accurately determined only by the post-operative histories. This fact puts the problem in a field of research which belongs to the surgeon, and forces him to standardize his operative procedures to histologic findings. Only by such standardization will the clinician, the surgeon, and the surgical pathologist be able scientifically to coöperate in their efforts to render justice to the patient.

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Fig. 253.—(39909.) Mammary acinus showing two rows of cells; the dark cells of the inner row are the differentiated or secretory cells; the pale cells of the outer row are the cells of the stratum germinativum. Primary epithelial hyperplasia.
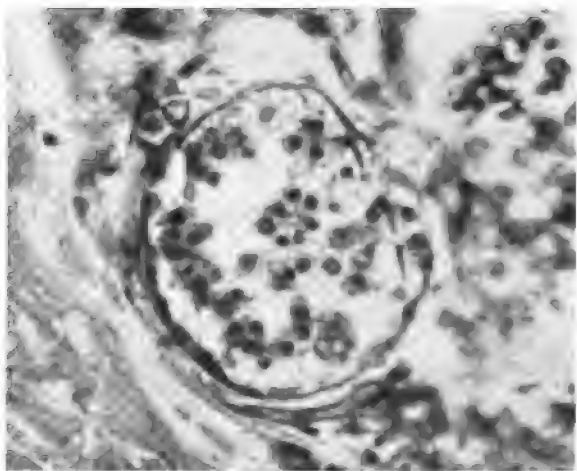
Fig. 254.—(28376.) Mammary acinus containing hyperplastic cells of the outer row (stratum germinativum). The cells of the inner row are absent. Secondary epithelial hyperplasia or precarcinomatous hyperplasia.
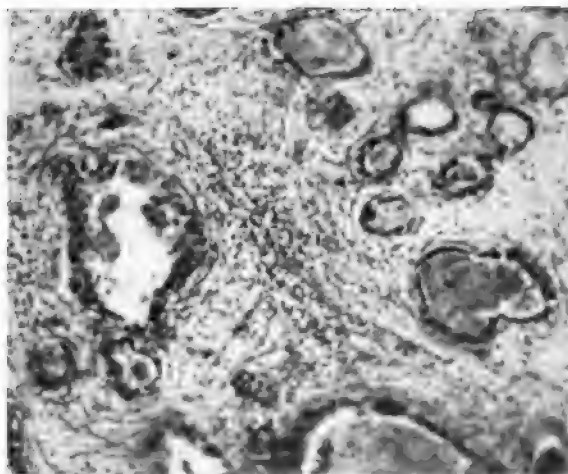
Fig. 255.—(36116.)   Secondary or precarcinomatous epithelial hyperplasia in the mammary gland.

PRIMARY, SECONDARY, AND TERTIARY EPITHELIAL HYPERPLASIA

a, Primary epithelial hyperplasia (not carcinoma)

b, Secondary epithelial hyperplasia (carcinoma?)

c, Tertiary or migratory hyperplasia (carcinoma)

Fig. 256.—(20797.)   Secondary or precarcinomatous epithelial hyperplasia in the mammary gland.
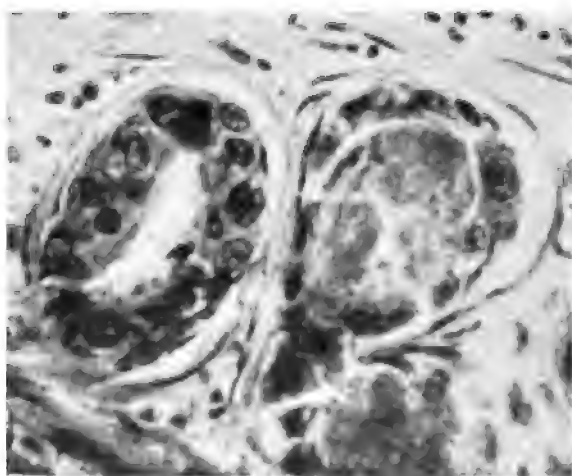
Fig. 257.—(36116.)   Mammary acini containing epithelial cells which are indistinguishable morpholog-
ically from extra-acinic cells of carcinoma.
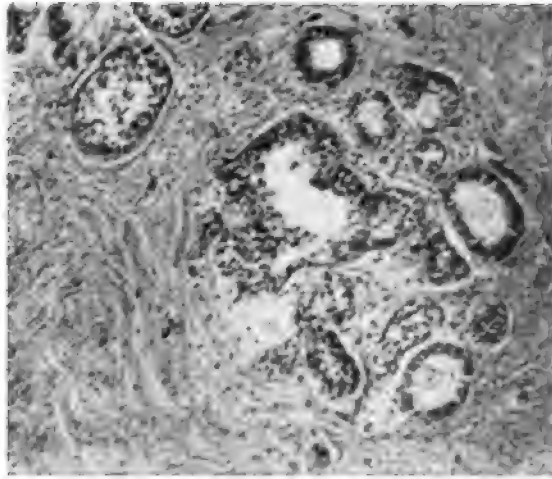
Fig. 258.—(35256.)   Secondary epithelial hyperplasia showing the indefiniteness of the line of demarcation between the stroma and the acinus.
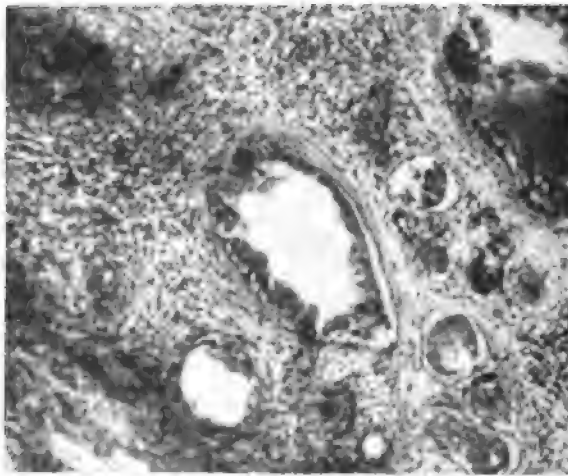
Fig. 259.—(36116.)   Secondary epithelial hyperplasia showing the indefiniteness of the line of demarcation between the stroma and the acinus.
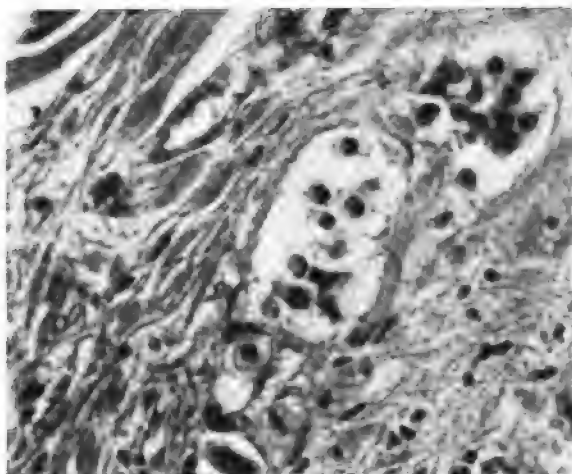
Fig. 260.
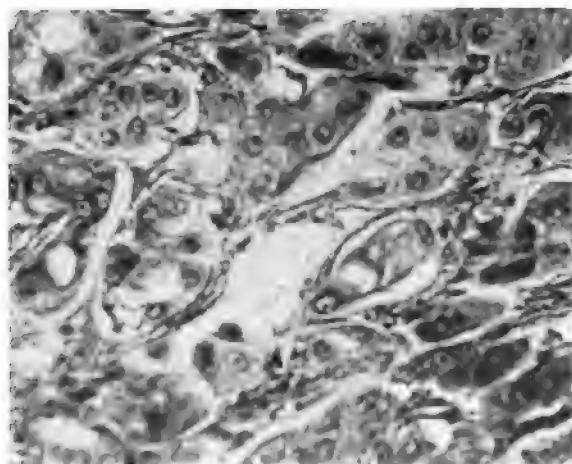
Fig. 261.

Figs. 260 and 261.—(31983.)   Tertiary or migratory epithelial hyperplasia (carcinoma) in a mammary gland.
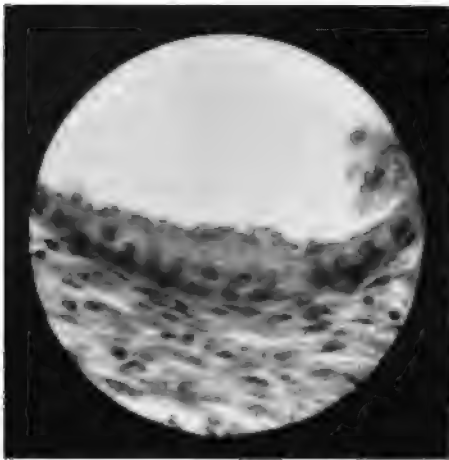
Fig. 262.—(15835.) Prostatic acinus, showing two rows of cells. The cells of the inner row are the differentiated or secretory cells; the cells of the outer row are the cells of the stratum germinativum. Primary epithelial hyperplasia.
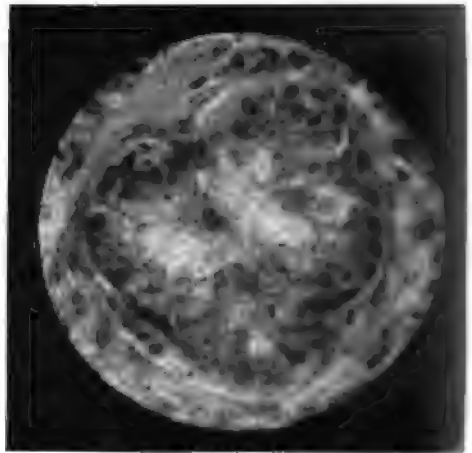
Fig. 263.—(15835.) Prostatic acinus. Secondary epithelial hyperplasia.

Fig. 264.—(15835.) Prostatic acinus. Secondary epithelial hyperplasia showing cells which are indistinguishable morphologically from carcinoma cells.

Fig. 265.—(15835.) Prostatic carcinoma (tertiary or migratory epithelial hyperplasia).
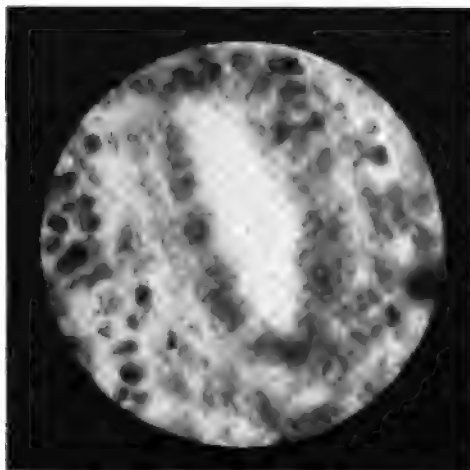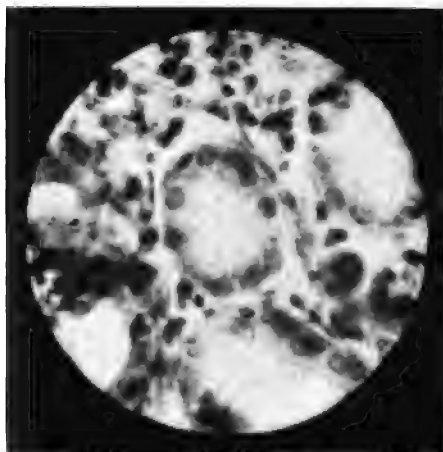
Figs. 266 and 267.—(53630.)   Epithelium in the border of the mucosa of a simple chronic gastric ulcer.

Fig. 268.—(53630.)   Epithelial hyperplasia in the border of a simple chronic gastric ulcer.   Secondary epithelial hyperplasia (?).
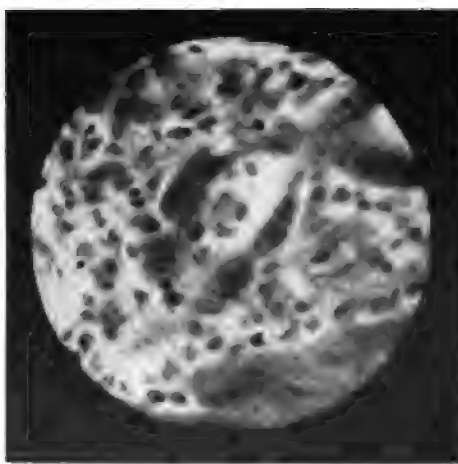
Fig. 269.—(35572.)   Tertiary epithelial hyperplasia in the gastric mucosa.
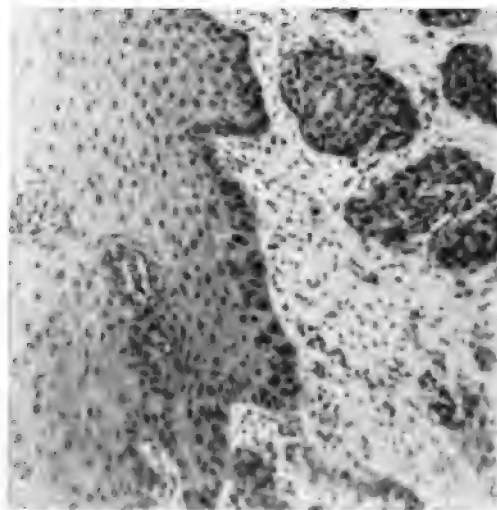
Fig. 270.
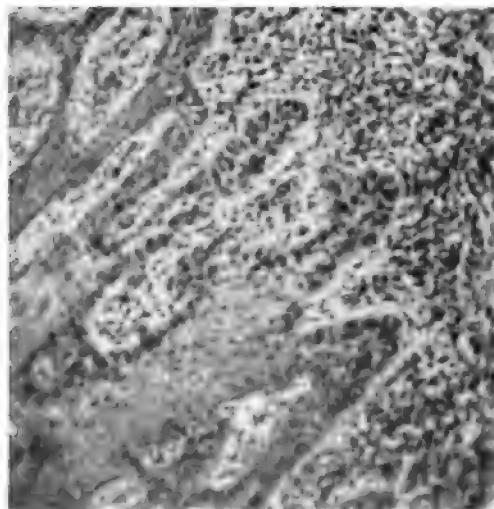
Fig. 271.

Figs. 270 and 271.—(A72606 and A77538.) Secondary epithelial hyperplasia in the stratum germi-
nativum of the skin of a lip.
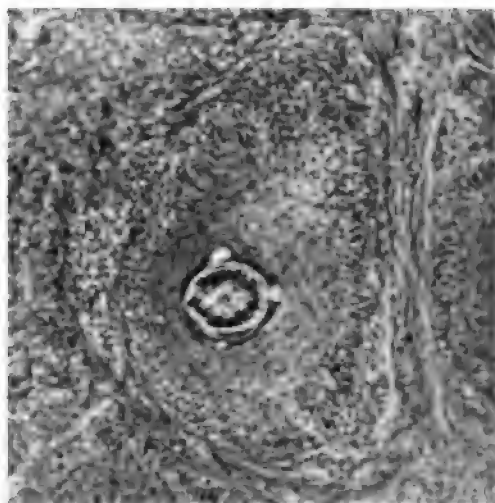
Fig. 272.—(A96196.) Secondary epithelial hyperplasia in the stratum germinativum of a hair-follicle.
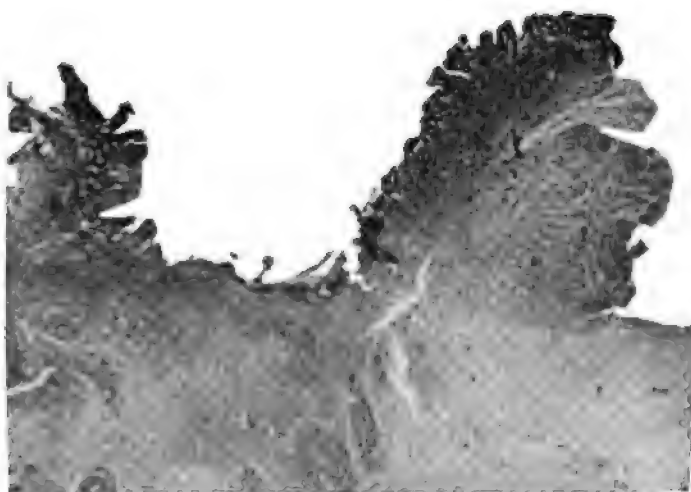
Fig. 273.—(53630.) Low-power photograph through a section of a simple chronic gastric ulcer.

Fig. 274.
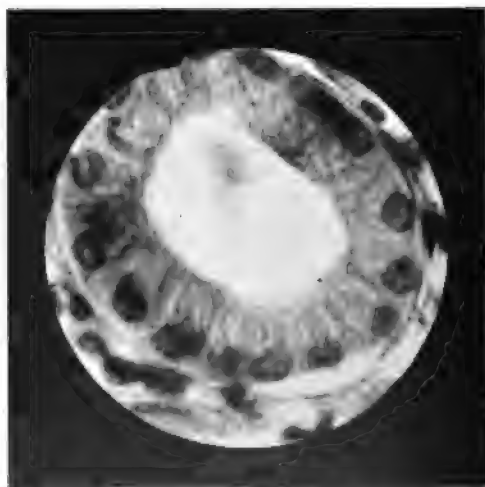
Fig. 275.

Figs. 274 and 275.—(48401, 49140.) Photographs through the border of a simple chronic gastric ulcer. The glands are regular, and show little or no distortion. The cells are regularly arranged around the lumen. The nuclei occupy a basal position in the cells.
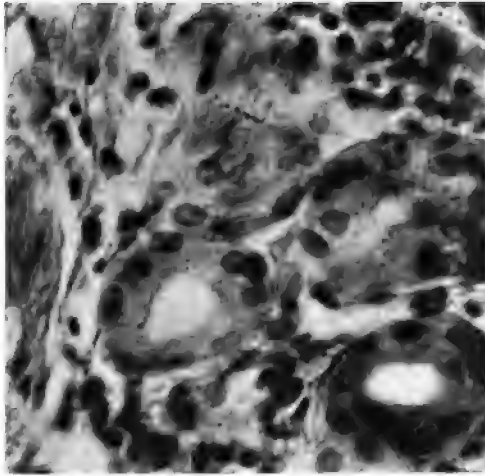
Fig. 276.—(52974.) Photographs through the same border from which Figs. 274 and 275 were taken. The cells do not present the regularity of arrangement seen in Figs. 274 and 275. The nuclei are not regularly placed at the bases of the cells. They vary in size and shape.
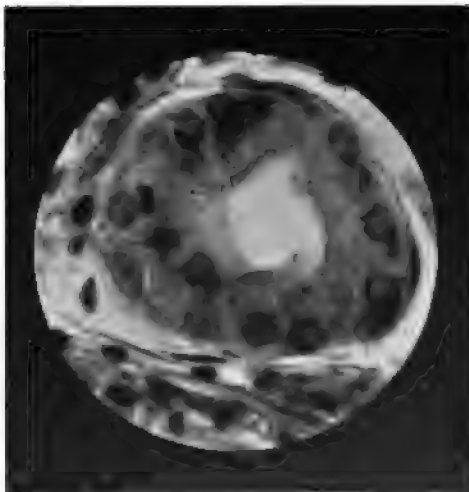
Fig. 277.—(49140.) Several glands showing the same cytologic changes which are seen in Fig. 276. This picture is frequently found in simple chronic gastric ulcers, and presents the same cellular appearance which is seen in secondary epithelial hyperplasia in the breast, prostate, skin, and hair-follicle.
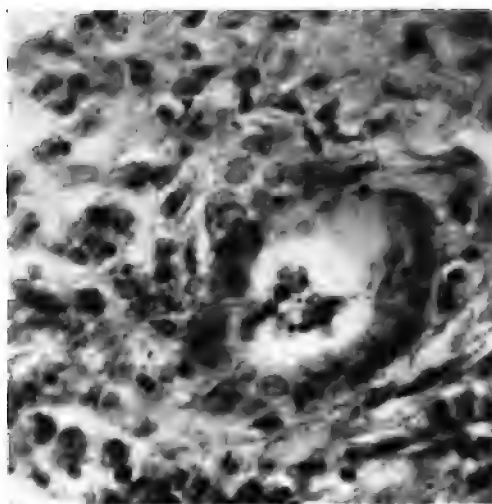
Fig. 278.
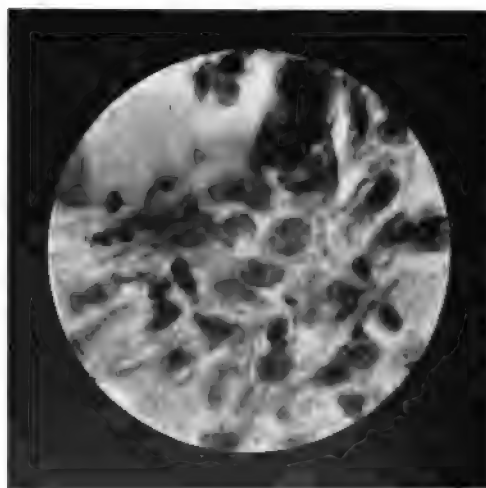
Fig. 279.

Figs. 278 and 279.—(52974.)   Intraglandular epithelial hyperplasia similar to that in Figs. 276 and 277, plus extraglandular epithelial cells which are morphologically similar to the intraglandular cells.
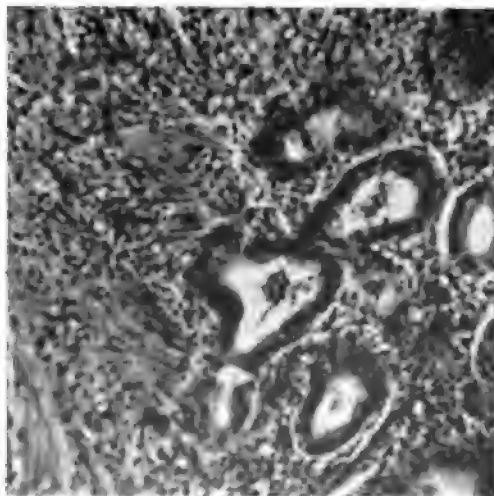
Fig. 280.
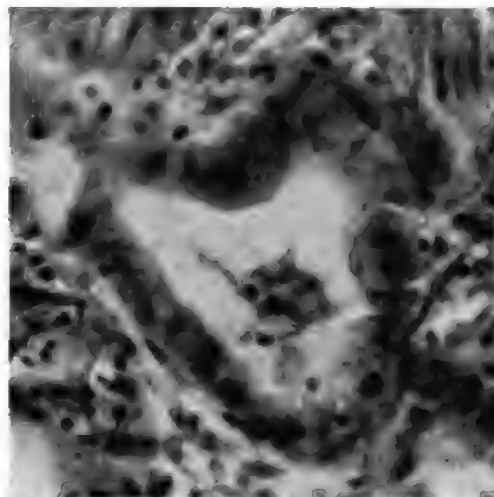
Fig. 281.
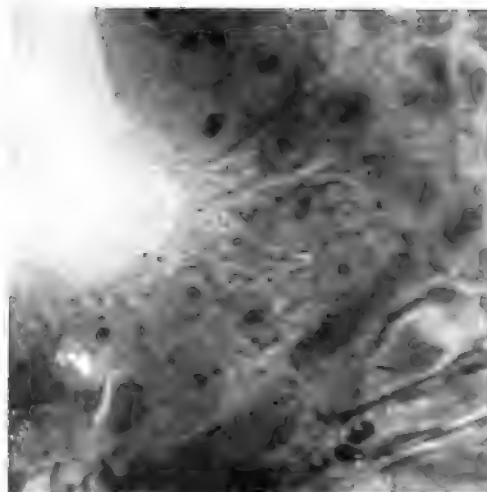
Fig. 282.

Figs. 280, 281, and 282.—(41681.)   Three magnifications of the same gastric gland, showing an intraglandular cytoplasm in the mucosa of a chronic gastric ulcer.   The cells, if compared with those in Figs. 283 and 284, will be found to be indistinguishable.
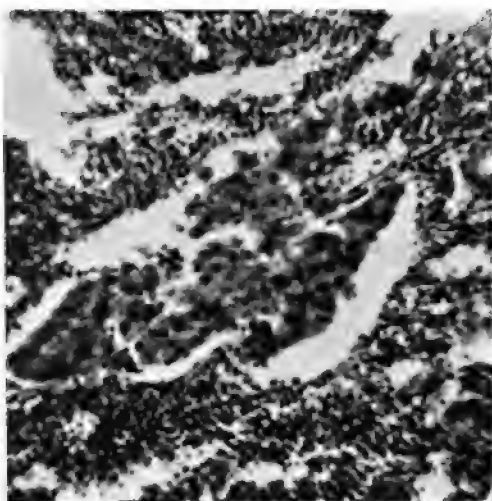
Fig. 283.
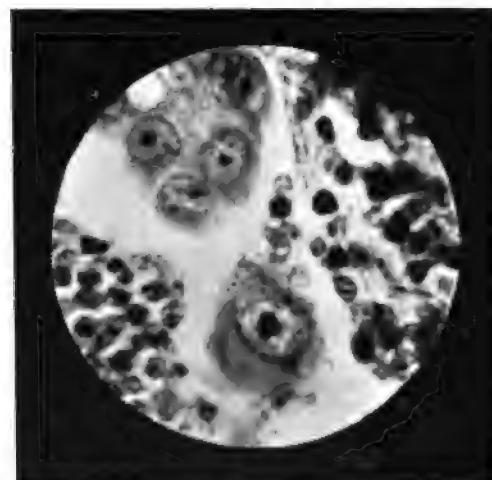
Fig. 284.

Fig. 285.

Figs. 283, 284, and 285.—(A57937.) Cells from a carcinomatous involvement in a subpyloric lymph-gland in a case of gastric carcinoma. The cells are morphologically indistinguishable from the cells of an intraglandular cytoplasm, which is frequently seen in simple chronic gastric ulcers.
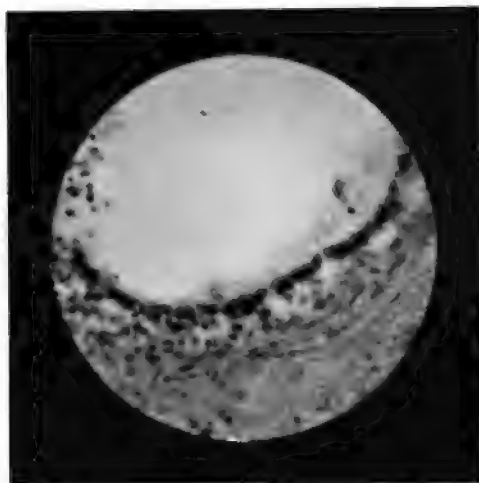
Fig. 286.—(56883.) Primary epithelial hyperplasia in mastitis chronica.
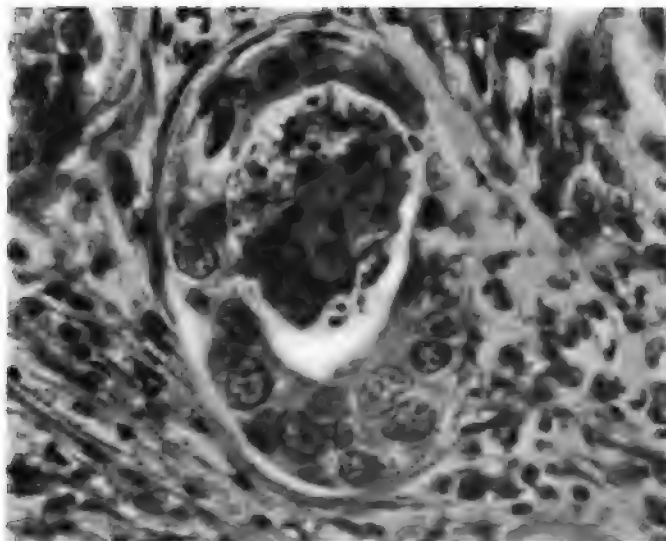
Fig. 287.—(56116.) Secondary epithelial hyperplasia showing cytologic characteristics.
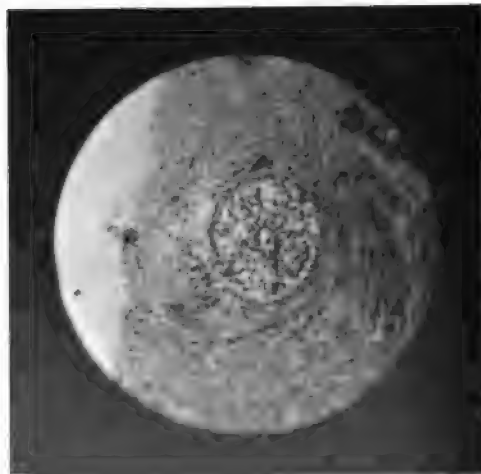
Fig. 288.
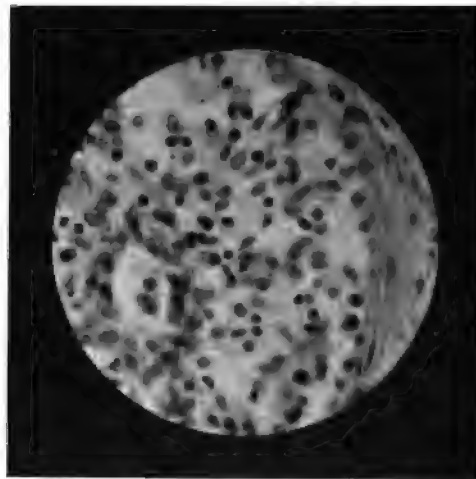
Fig. 289.
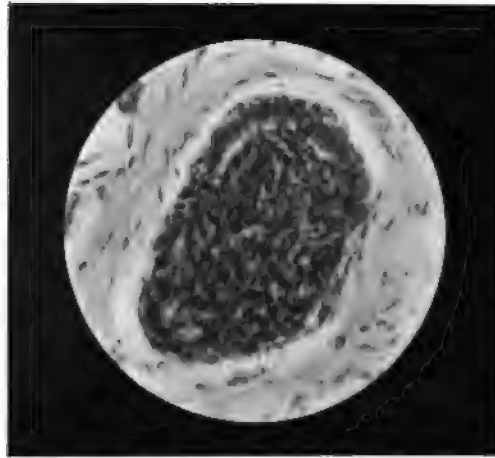
Fig. 290.—(17411.) Primary and secondary epithelial hyperplasia in the same acinus, from a specimen of mastitis chronica.

Figs. 288 and 289.—(56883.) Secondary epithelial hyperplasia in mastitis chronica.
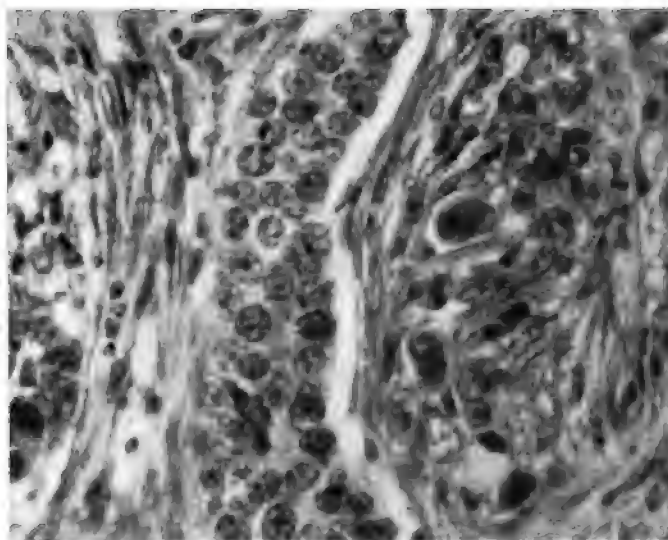
Fig. 291.—(31329.) Tertiary epithelial hyperplasia (carcinoma). Cells in a lymph-space.
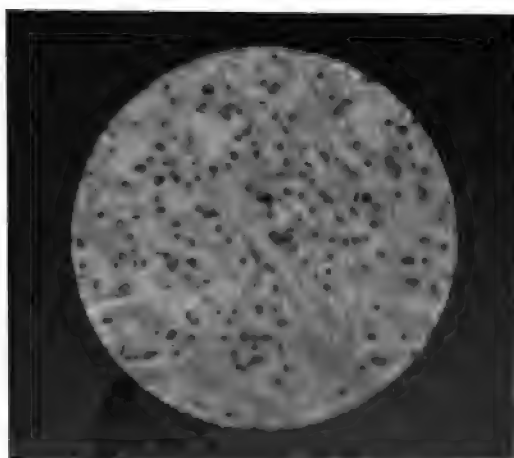
Fig. 292.—(56383.) Tertiary epithelial hyperplasia in mastitis chronica.
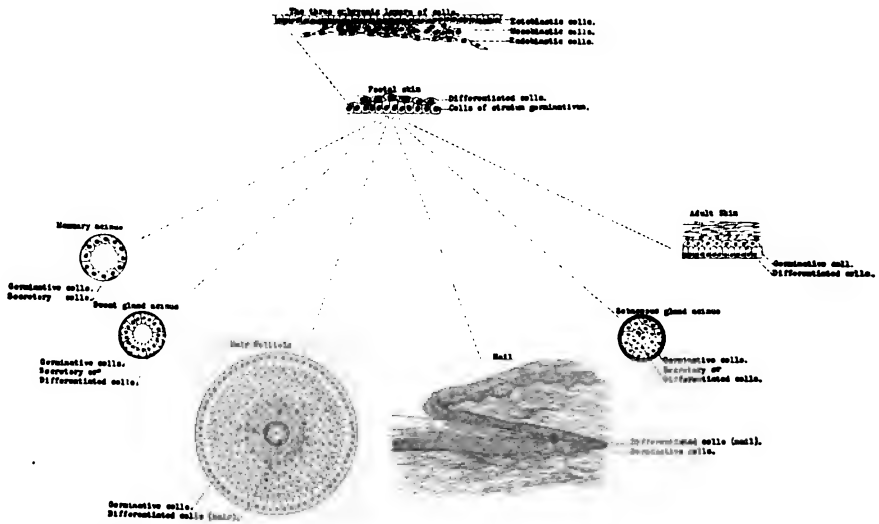
Fig. 293.—Organic differentiation of the ectoblastic cells. The ectoblastic cells become differentiated into the cells of the stratum germinativum of the embryonic skin. The cells of the stratum germinativum become further differentiated into the germinal cells of the mammary glands, sweat-glands, sebaceous glands, hair, nails, and epidermis. The germinal cells of these organs become further differentiated into the milk-producing cell of the breast, the sweat-producing cell of the sweat-gland, the fat-producing cell of the sebaceous gland, the hair of the skin, the nails of the skin, and the epidermis of the skin.
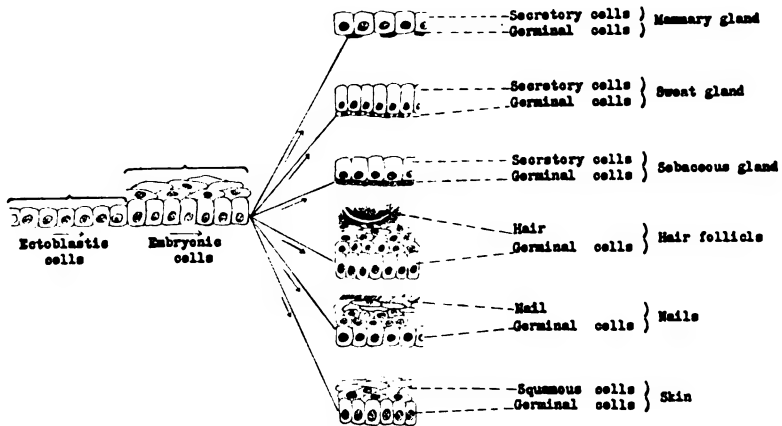
Fig. 294.—Cytologic differentiation of the ectoblastic cells. The ectoblastic cells become differentiated into the cells of the stratum germinativum of the embryonic skin. The cells of the stratum germinativum become further differentiated into the germinal cells of the mammary glands, sweat-glands, sebaceous glands, hair, nails, and epidermis. The germinal cells of these organs become further differentiated into the milk-producing cell of the breast, the sweat-producing cell of the sweat-gland, the fat-producing cell of the sebaceous gland, the hair of the skin, the nails of the skin, and the epidermis of the skin.
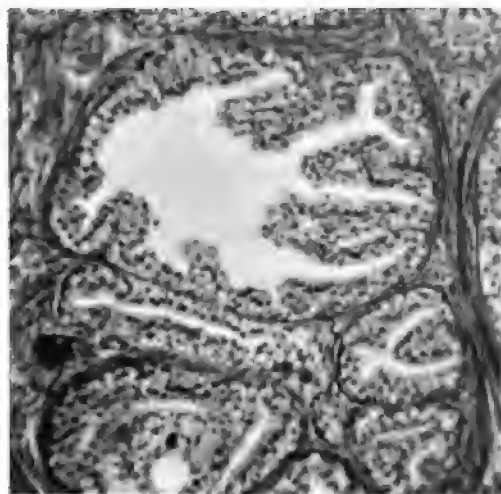
Fig. 295.
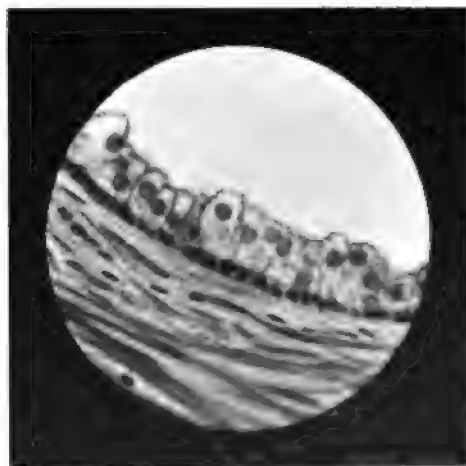
Fig. 296.

Figs. 295 and 296.—(16846.) Primary epithelial hyperplasia in a prostatic gland (prostatitis chronica).
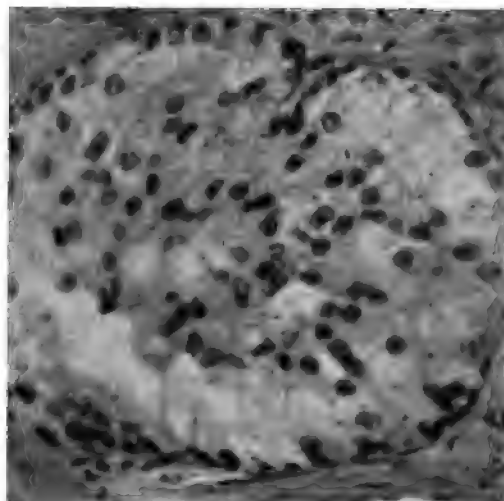
Fig. 297.
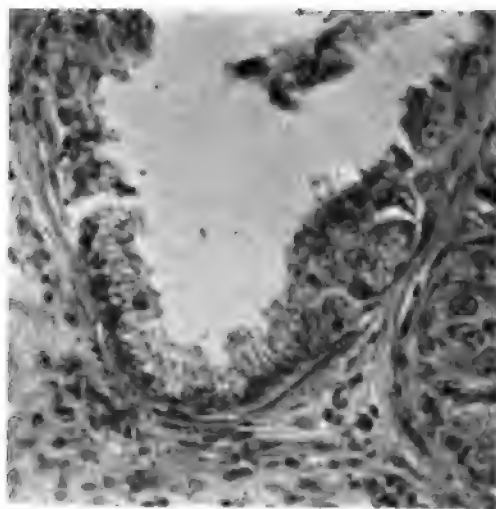
Fig. 298.

Figs. 297 and 298.—(41396, 15835.) Secondary epithelial hyperplasia in prostatitis chronica.
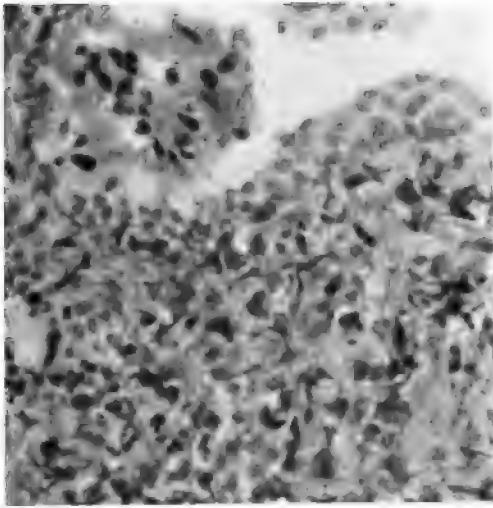
Fig. 299.—(44396.)   Tertiary epithelial hyperplasia (carcinoma) in prostatitis chronica.
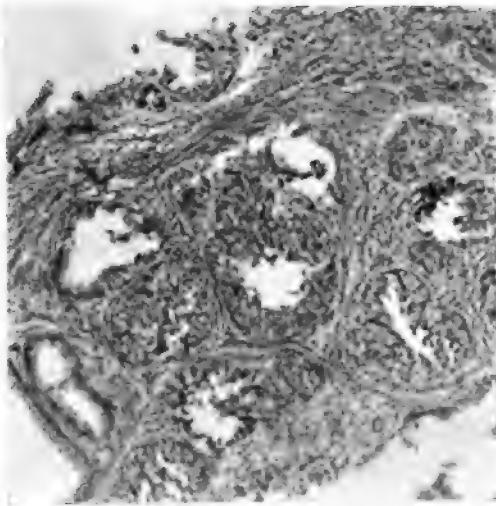
Fig. 300.—(15835.)   Primary, secondary, and tertiary (carcinoma) epithelial hyperplasia in prostatitis chronica.

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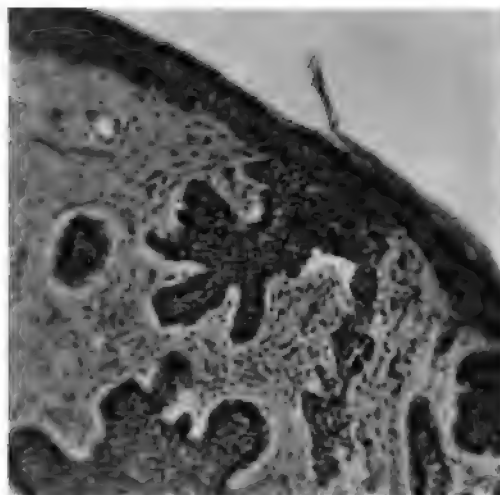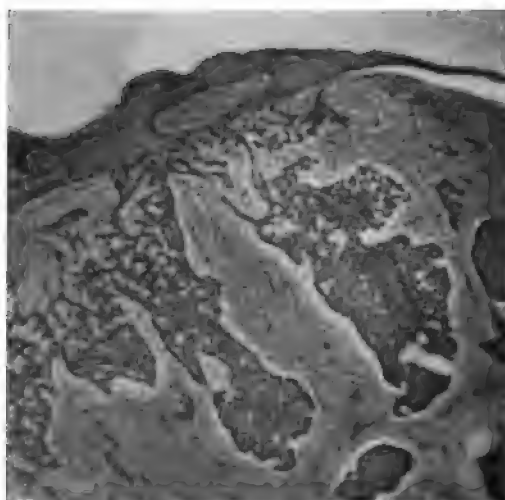
Fig. 301.

Fig. 302.

Figs. 301 and 302.—(8626, 71769.) Tertiary epithelial hyperplasia (epithelioma) in dermatitis chronica.
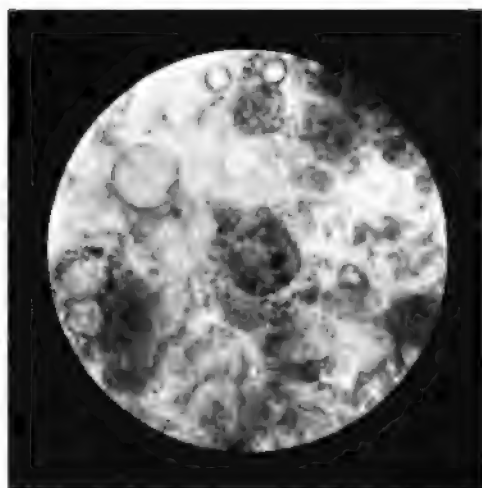
Fig. 303a.—(116794.) Bladder. Shows characteristic cancer-cells from different organs. Many of them are perfectly round and show clearly the nuclei and nucleoli.
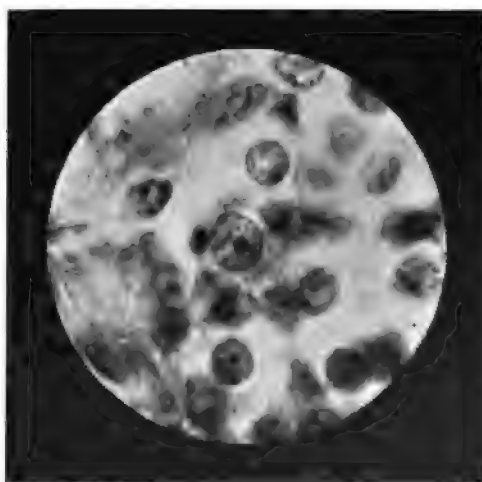
Fig. 303b.—(69577.) Breast.

Fig. 303c.—(71483.) Breast.
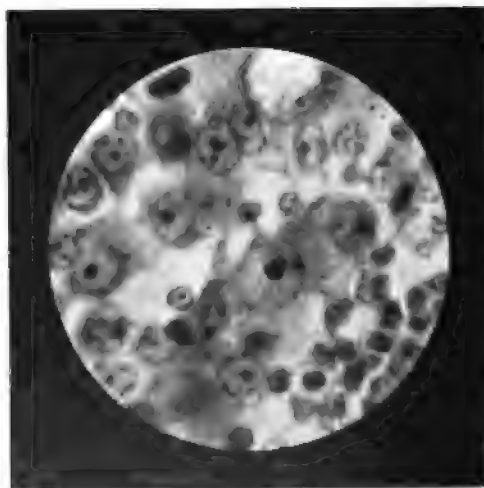
Fig. 303d.—(37237.) Stomach.
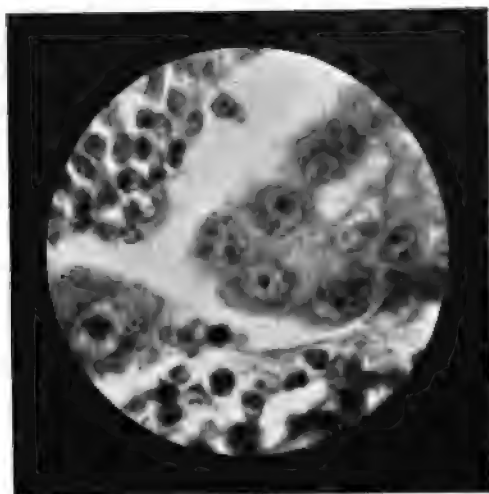
Fig. 303e.—(37237.) Stomach.

Fig. 304a.—(73588.) Breast. Characteristic cancer-cells, some round and some oval, showing the destruction of the cytoplasm and irregularities of the nuclei and nucleoli resulting from cytolysis and pressure.
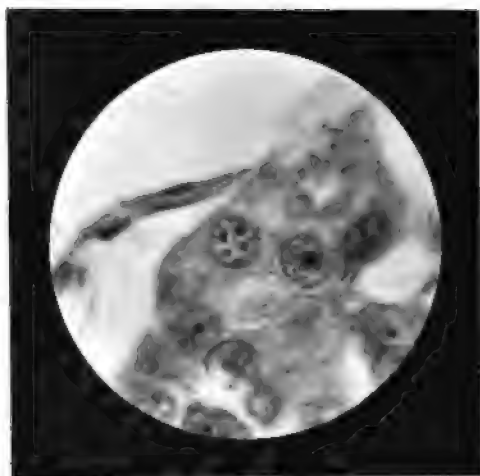
Fig. 304b.—(17483.) Breast.
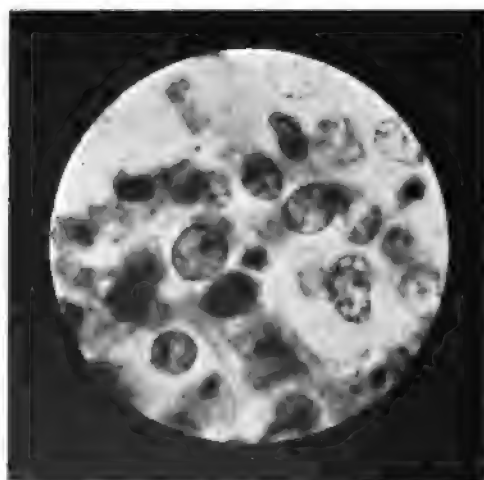
Fig 304c.—(69577.) Breast.
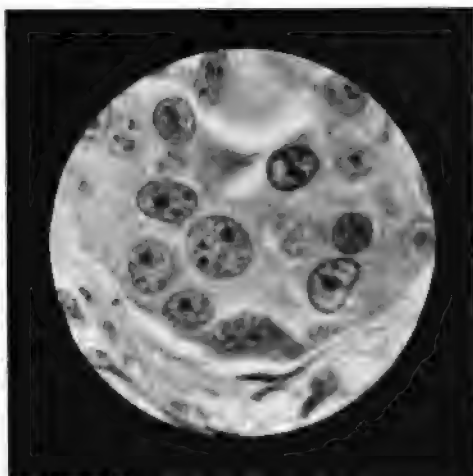
Fig. 304d.—(A71483.) Breast.
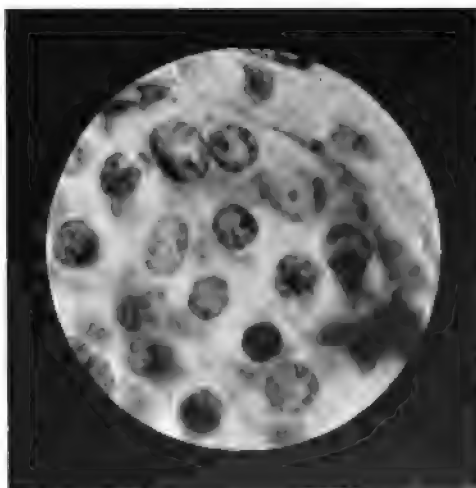
Fig. 304e.—(69577.) Breast.
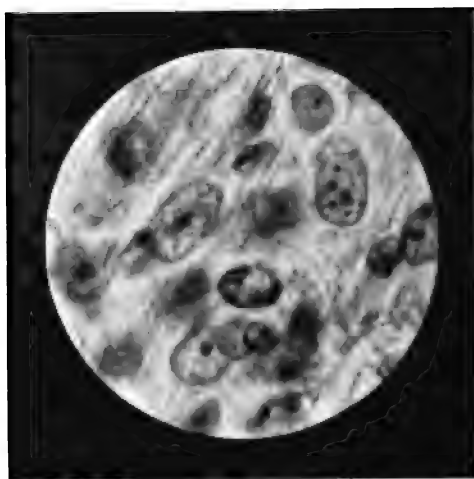
Fig. 304f.—(69577.)   Breast.
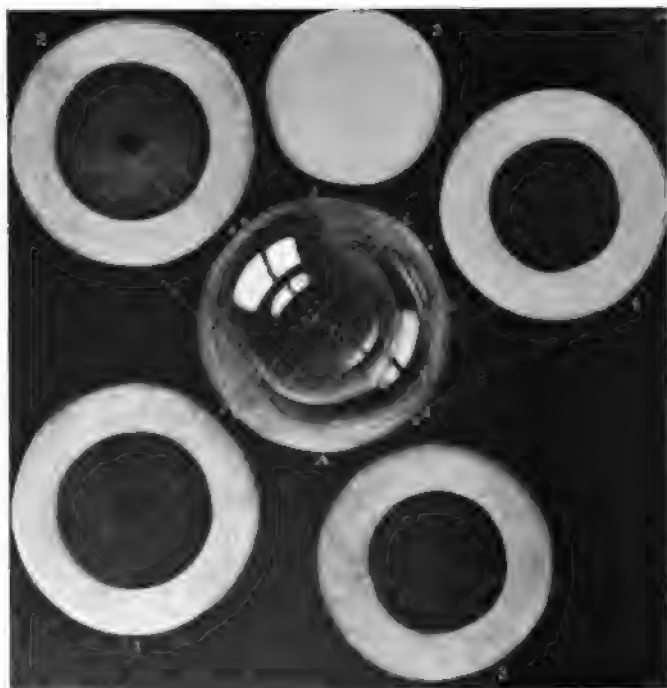
Fig. 305.—Spheric cells, showing the nuclei and nucleoli. The cells have been cut in various planes. The variation of size and shape of the planes with and without nuclei and nucleoli accounts for some of the irregularities of size and shape which are seen in the cancer-cell in sections of cancerous tissue. The majority of cancer-cells of perfectly fresh tissue are practically as regular in shape as the drawings in this diagram.

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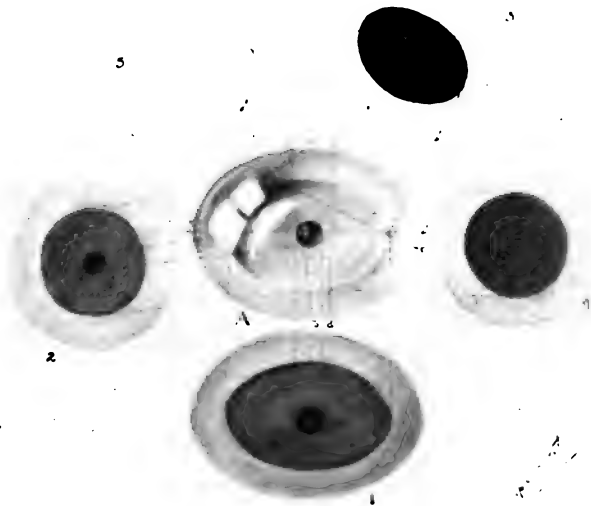
Fig. 306.—Oval cells showing the nuclei and nucleoli. The cells have been cut in various planes. The variation of size and shape of the planes with and without nuclei and nucleoli accounts for some of the irregularities of size and shape which are seen in the cancer-cell in sections of cancerous tissue. The majority of cancer-cells of perfectly fresh tissue are practically as regular in shape as the drawings in this diagram.
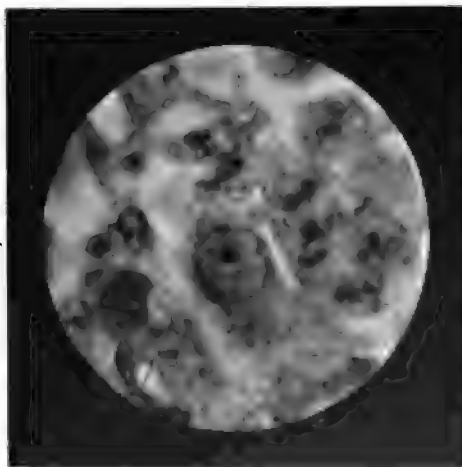
Fig. 307a.—(A8526G.) Sigmoid. Characteristic cells of gastric intraglandular hyperplasia (secondary hyperplasia), carcinoma of the breast, secondary carcinoma of a gastric lymphatic gland, and carcinoma of the sigmoid, all of which cells are morphologically indistinguishable.

633
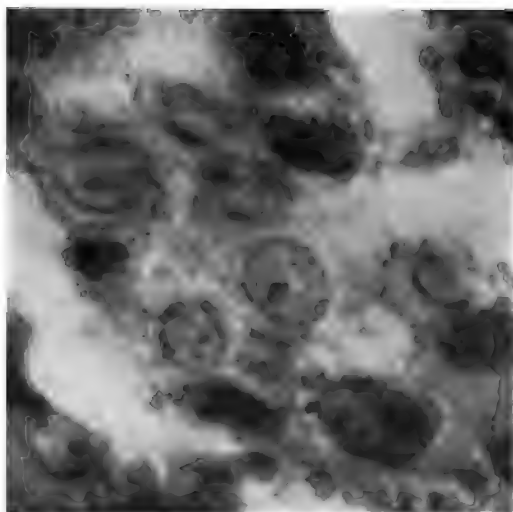
Fig. 307b.—(50647.)   Breast.   (See legend 307a.)
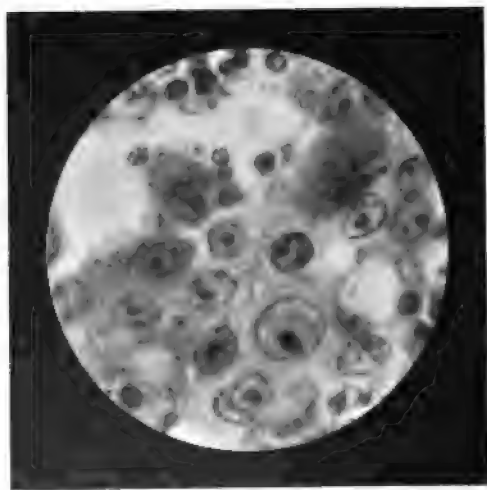
Fig. 307c.—(37237.)   Stomach.   (See legend 307a.)
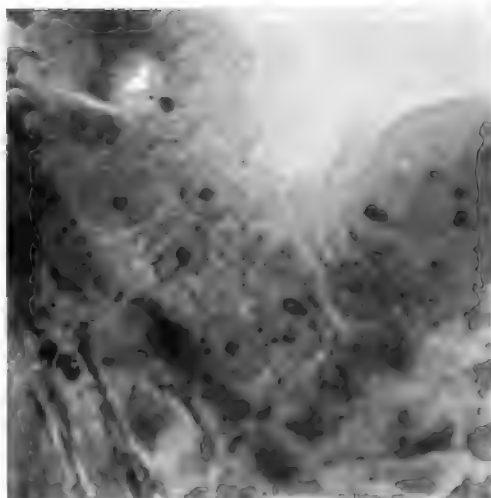
Fig. 307d.—(41681) Stomach. (See legend Fig. 307a.)
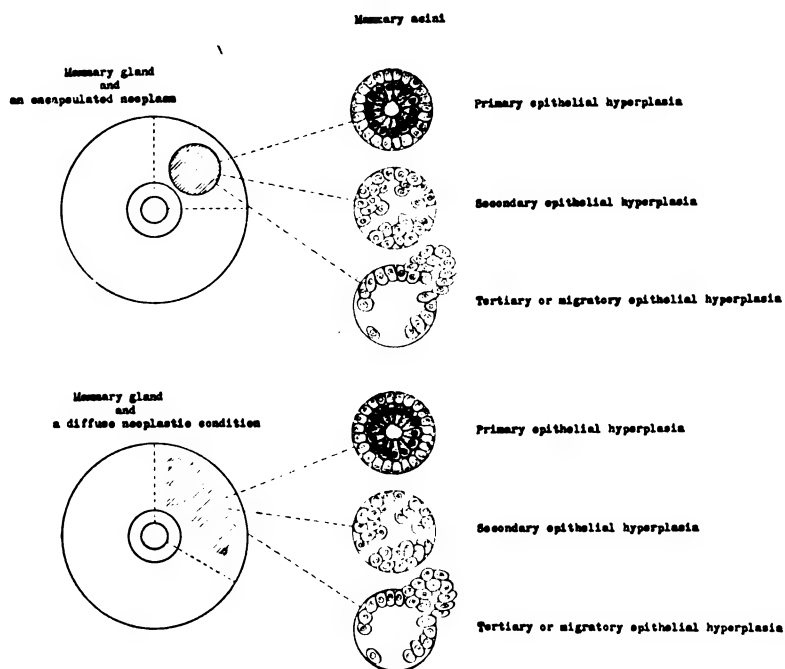
Fig. 308.—Encapsulated and diffuse fibro-epithelial neoplasia, showing the histologic pictures of primary, secondary, and tertiary (carcinoma) epithelial hyperplasia.

Mammary and prostatic acini
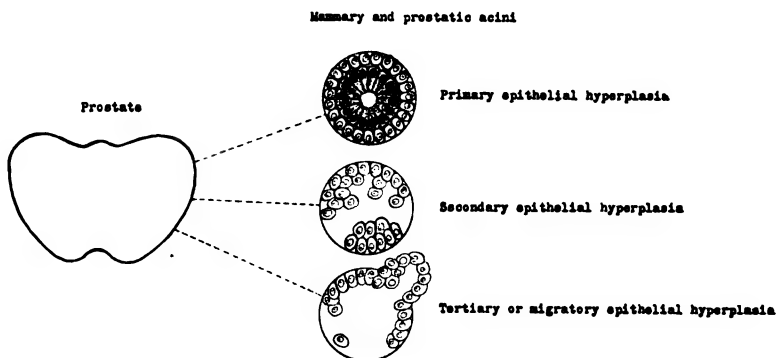
Fig. 309.—The prostatic epithelium presents the same arrangement of cells with the same cytologic characteristics which are found in the breast.
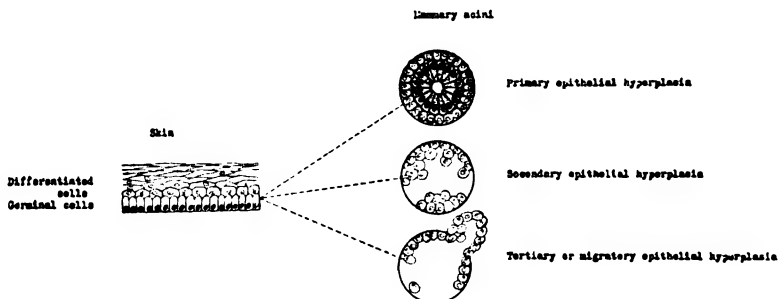
Fig. 310.—The principal cytologic changes which occur in the hair-follicle in chronic dermatitis are seen in the germinal cells, which present the same cytologic characteristics which are seen in the mammary acini when undergoing a condition of epithelial hyperplasia.
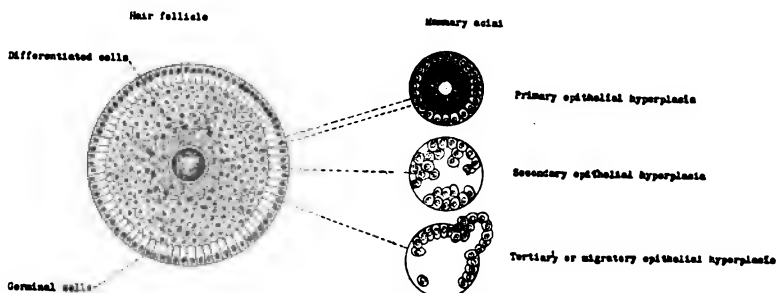
Fig. 311.—In conditions of chronic folliculitis one finds the most marked cytologic activity in the germinal layer of cells, which present the same cytologic characteristics which are seen in secondary and tertiary epithelial hyperplasia in the acini of the mammary gland.
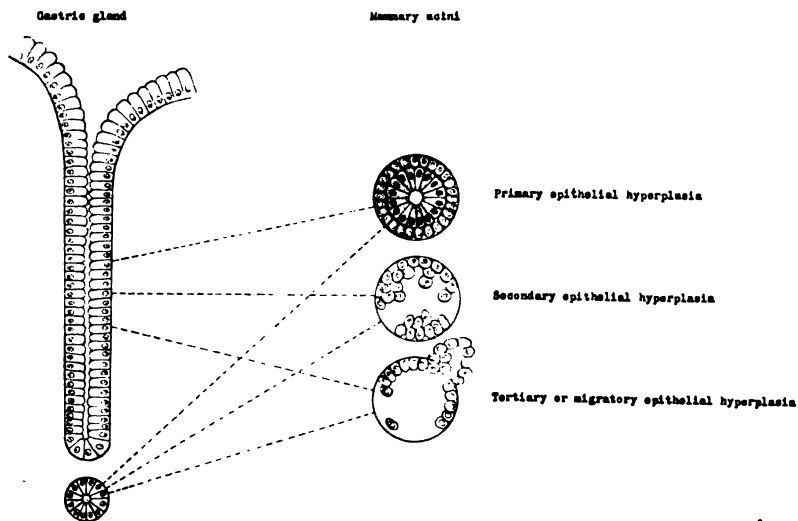
Fig. 312.—The analogy between the observations of epithelial hyperplasia in the breast and those in the stomach. The location of the germinal cells in the gastric gland is at present uncertain. In the gastric gland two rows of cells are not seen, as in the prostate, breast, skin, and hair-follicle. However, where the differentiated columnar or cuboid gastric epithelial cells are normal, one sees, in chronic inflammatory conditions, certain cytologic pictures which are analogous to those which are seen in secondary and tertiary epithelial hyperplasia in the breast.

THE PATHOGENESIS OF CANCER OF THE PROSTATE*

BERNARD FRANCIS McGRATH

The facts that the general subject of cancer presents even to-day one of our most serious and unsolved problems; that cancer of the prostate is a comparatively frequent and exceedingly distressful form of the disease; and the probability that by a more widespread application of the present available knowledge of this pathologic process the prevalent high percentage of disability and death would be considerably diminished, are advanced as sufficient reasons for presenting a discussion of the subject with a contribution of data to the fund of experience.

The pathogenesis of cancer of the prostate is still a debatable question; the frequency of its occurrence, the usual sites of its original focus, its mode of extension and metastasis, are phases of the subject which are reasonably supported by facts.

This paper is based, first, on the examination of a series of 716 prostatic specimens removed at operation in the Mayo Clinic from October 28, 1904, to June 1, 1914; second, on the pathogenesis of epithelial tumors of the breast, as viewed by MacCarty; and third, on a review of the literature.

PATHOGENESIS

The opinions of various investigators with regard to the pathogenesis of cancer of the prostate are not uniform. The cause of this lack of uniformity seems to be due, at least in a great measure, to the different points from which the pathologic process is viewed.

Some authors maintain that cancer does not begin in a hypertrophic portion of the gland, that its presence here is an invasion from a focus situated elsewhere in the organ, usually in the posterior lobe. Others state that cancer occurs as an almost imperceptible transition from a benign adenoma. Still others, disregarding as unessential the consideration whether the associated process be one of general hypertrophy, adenoma, or other pathologic condition, view, apart from its causation, the pathogenesis of prostatic cancer, likewise of cancer in general, as fundamentally a question of the histogenesis of epithelial cells.

A summation of the evidence adduced from the various investigations emphasizes the fact that cancer occurs in the atrophic, the apparently normal, and the hypertrophic prostate. In the light of this accepted fact is seen an indication that, involved in the development of the cancerous process, there is a study far more basic than what is comprehended in a consideration of associated pathologic conditions. Again, the weight of evidence seems to prove that the disease begins most frequently in the posterior lobe of the gland. This seeming selectiveness of the process, however, is no more explicable in the prostate than are similar phenomena in other organs. The incident of original focus is aside from the underlying principle of pathogenesis, as advanced in the theory of the histogenesis of epithelial tissue.

CANCER OF THE BREAST

In 1898 Albarran and Hallé,[1] in an oft-quoted and adversely criticized treatise, under the caption, "Hypertrophy and Epithelial Neoplasms of the Prostate," direct attention to the "remarkable *analogy between the hypertrophied prostatic gland and the mammary gland* affected with benign tumors, or with those epithelial and interstitial lesions which are still wrongly classified among the benign neoplasms and the chronic inflammations."

In 1907 Ewing,[2] discussing "Cancer Problems," stated that "inflammatory hyperplasia passes by insensible gradations into neoplastic growths."

During the past five years MacCarty[3] has contributed several

papers to the subject of cancer of the breast. This author was stimulated to undertake an extensive investigation of the epithelial growths of the mammary gland, because of inability to harmonize his daily observations with the prevalent views of the pathogenesis of these tumors and the apparently redundant, diverse, and unintelligible classification of the pathologic processes.

At the beginning of this work the hypothesis was formulated that the cells of cancer are the direct offspring of cells normally present in the acinus of the breast, and that they are derived neither from the differentiated cells through metaplasia, nor from prenatal or postnatal rests, according to the views attributed to Cohnheim and Ribbert. The investigation has been pursued on the foundation constructed by authoritative embryologists; personal speculation has been scrupulously avoided, and notes of conditions have been confined strictly to the morphologic evidence presented by epithelial tissue under the microscope.

At the present period of this long investigation MacCarty states that his earlier observations have been confirmed, and that his view of the origin of cancerous cells in the breast is no longer a hypothesis, but a demonstrable fact.

With the purpose of endeavoring to determine an analogy between the pathogenesis of cancer of the mammary gland, as advanced by MacCarty, and the pathogenesis of cancer of the prostate, I undertook the examination of this series of prostatic specimens.

A brief summary of MacCarty's investigation of epithelial growths of the breast follows:

The normal acinus of the mammary gland is lined with a single row of cylindric epithelial cells, which are the differentiated, functional cells of the organ. These differentiated cells arise from the stratum germinativum, which is usually undiscernible until some stimulus causing hyperplasia is present. Then the germinative layer appears in the acinus as a second row of cells which adjoins immediately the surrounding stroma. For descriptive purposes these cells are termed the outer row, and are described as the undifferentiated or partially differentiated precursors of the specific

functional cells. The morphologic appearance of these cells of the outer row differs from that of the differentiated cells, which now form and are termed the inner row. In the presence of an excessive or abnormal stimulus the cells of the outer row become hyperplastic and partially or completely fill the acinus. In this event the functional cells are present, exfoliated, or absent. Furthermore, the undifferentiated cells are observed not only intra-acinic, but also extra-acinic, situated in the stroma. Therefore, some microscopic fields present both rows of cells, differentiated and undifferentiated, distinct in the acinus; other fields show a definite predominance of intra-acinic, hyperplastic undifferentiated cells; and in still others, both intra-acinic and extra-acinic hyperplastic undifferentiated cells are seen. In some fields in which the inner row of functional cells are exfoliated or absent, and the undifferentiated cells of the outer row hyperplastic, the line of demarcation between the acinus and the stroma is observed obliterated, totally or in part, and the latter cells are noted also in the stroma. The facts that epithelial invasion of stroma is the accepted histologic picture of cancer; that in these observations the epithelial cells in the stroma are morphologically indistinguishable from the hyperplastic undifferentiated cells of the acinic outer row; and, finally, that the latter cells represent the normal precursors of the functional cells in the stratum germinativum, seem to lead logically to the deduction that *the cancerous cells of the mammary gland are the direct, immediate descendants of the undifferentiated cells of the germinative layer*, consequently, that the hypothesis of "embryonic rests" is not essential for the explanation of cancer in this organ.

For the sake of simplicity in studying the mammary epithelial tumors, the following classification is based on the observations cited above: The pathologic processes involved in these epithelial growths are designated: (1) Primary hyperplasia; (2) secondary hyperplasia; (3) tertiary or migratory hyperplasia. In primary hyperplasia both rows of cells, the inner, differentiated, and the outer, undifferentiated, are present and concerned in the reaction; in secondary hyperplasia, the outer row, undifferentiated cells,

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these cells are termed the outer row, and are described as the un-
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the outer row differs from that of the differentiated cells, which
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excessive or abnormal stimulus the cells of the outer row become
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hyperplasia; (3) tertiary or migratory hyperplasia. In primary
hyperplasia both rows of cells, the inner, differentiated, and the
outer, undifferentiated, are present and concerned in the reaction;
in secondary hyperplasia, the outer row, undifferentiated cells,

    '14—41

are excessively proliferated (cancer?); in tertiary hyperplasia the hyperplastic undifferentiated cells of the outer row are also present in the stroma (cancer).

The probability is advanced that, viewed in the light of these studies, the old criterion for determining cancer histologically, namely, the permeation of the "basement-membrane," may be erroneous, consequently that we may be compelled to view the condition of secondary hyperplasia as possibly malignant before invasion of tissue has occurred.

Cancer of the Prostate

In examining the prostatic specimens of this series for the purpose of seeking an analogy between the cancerous process in this gland and that noted by MacCarty in the breast, the following observations have been made:

The normal acinus of the prostate is lined with a single or an imperfect double layer of columnar epithelial cells. These are the differentiated or specific functional cells of the gland. In the examination of the pathologic specimens these functional cells are seen frequently in a state of excessive proliferation, forming projections in and bridges across the acini. There is observed also partial or complete exfoliation of the same cells with the formation of cysts, which are empty or contain accumulations of the cells in varying degrees of degeneration. Some fields are noted in which the acini present not only the proliferated functional cells, but also, outside these and immediately adjoining the stroma, another row of cells which are morphologically dissimilar to the inner row of differentiated cells. Other fields contain acini with functional cells present, exfoliated or absent, and the lumina partially or completely filled with the hyperplastic undifferentiated cells of the outer row. Still other fields are seen in which these hyperplastic cells of the outer row are both intra-acinic and extra-acinic, consequently presenting epithelial invasion of tissue, the accepted picture of cancer. Furthermore, what is impressive, the three conditions just described have been observed together in the same microscopic field.

An analysis of this comparative study of the prostate and the mammary gland indicates that an analogy exists between the microscopic pictures of epithelial changes in the cancerous process of both organs. The analogy being accepted, it follows that this study of the prostate adds further support to MacCarty's deduction, drawn from extensive observations on epithelial growths of the breast. If adequately prolonged and comprehensive investigations in the future positively confirm the present view of the latter author, it may be stated of the prostate that, whatsoever the associated pathologic condition or wheresoever the original focus, these are factors which are unessential to the process of cancerous development; that this is essentially a process of epithelial hyperplasia, involving the above-described undifferentiated cells, in a state of reaction to an abnormal irritant. Furthermore, for the pathogenesis of cancer it would not be necessary to assume the theory of "embryonic rests."

Frequency.—Statistics indicate that we are indebted to the investigators of the past half century for the existing knowledge of cancer of the prostate. The first useful statistics were compiled by Thompson[4] (1854), who cited 18 cases from the English and the French literature. Wyss[4] (1866) reported 28 cases, including Thompson's; Socin[4] (1875), 50 cases; Kapuste[4] (1885), 54 cases; Engelbach[4] (1888), 144 cases; Wolff[5] (1899), 110 cases. Since 1902, numerous reports of malignant prostatic conditions have been contributed. It is the statistics of the more recent writers, however, which, although varying within somewhat wide limits, afford us the nearest approximation to the truth with regard to the frequency with which cancer occurs in the prostate.

In 500 cases of prostatic obstruction Young[6] found cancer in 20 per cent. The same author states that about one out of every seven enlarged prostates after fifty years of age is cancerous. Albarran and Hallé noted 14 per cent.; Walker,[7] 16.5 per cent.; Wilson and McGrath[8] (1911), 468 reëxamined prostatic specimens removed at operation, 15.5 per cent.; Freyer[9] (1914), 1276 cases of enlarged prostate, 13.3 per cent. In the present series of 716

specimens (including the 468 cases reported by Wilson and Mc-Grath in 1911), 12.28 per cent.* are cancer.

Age.—One patient was between the ages of forty and fifty. Seventy-eight per cent. were between sixty and eighty. Other investigators have found about 68 per cent. between the ages of fifty and seventy. Wolff reports 6 patients under forty; 1, twenty-nine years of age.

Mode of Involvement.—Cancer of the prostate is primary in the great majority of cases. The gland is involved secondarily by adjacent cancer or through metastasis by way of the blood-stream. Rectal ulceration is the most frequent source of secondary prostatic cancer from contiguous structures. About one-half the cases of secondary involvement are metastatic from remote organs.

Site of Origin.—The most commonly ascribed site of the original focus in primary cancer of the prostate is the posterior lobe; but its presence in the lateral and middle lobes has been noted by some authors.

Growth.—The cancerous process has been observed to involve the entire prostate symmetrically and rapidly, but the consensus of investigators' opinions is that in by far the large proportion of cases cancer of this gland is limited, occurring as one or several little nodules and of slow growth. Consequently, gross serial sections of the specimen and microscopic examination of every doubtful area are essential for the diagnosis in the great majority of cases. Failure to appreciate this point, also neglect to examine the posterior lobe, are the probable causes of statistics with low percentage of cancer, likewise of inadequate treatment and erroneous prognosis.

Extension.—In the extension of prostatic cancer the fascia of Dénonvilliers, also the fibrous capsules, both of the prostate itself and of hypertrophied spheroids, lobules, or lobes, are accredited with an essentially important rôle. Young emphasizes this point. Cunéo and Veau[10] have shown that the fascia of Dénonvilliers is a prolongation downward of the peritoneum in fetal life, which, projecting in a plane between the prostate and the seminal vesicles

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* In the last 248 cases of this series only the specimens already diagnosed cancer were studied. It is probable that reëxamination of the remaining specimens will increase the percentage of malignancy.

in front, and the rectum behind, by virtue of its reduplication, doubly inhibits the spread of cancerous cells posteriorly. Consequently, ulceration of the rectum is infrequently seen, and periprostatic structures are quite effectively guarded. The tendency, then, of the cancerous process is to extend upward to the region of the ejaculatory ducts, between the fascia of Dénonvilliers posteriorly and the trigone anteriorly. Young maintains that the mucosa and submucosa of both urethra and bladder are very resistant to the malignant invasion. On the other hand, von Frisch[11] notes extensive involvement of both these structures. The seminal vesicles are frequently involved, and the growth may extend along the ureters, causing complete obstruction, even rupture. Extension upward for a long distance within the vasa deferentia, without apparent involvement of the outer walls, may occur (Young). Cases noted by von Frisch were: Growth into rectum with subsequent extensive involvement of the sacrum. Growth through the obturator foramen and between the adductors of the thigh. Once the capsule is permeated, the cancerous process spreads extensively.

Metastasis.—This occurs in bones, lymphatic glands, and internal organs. Important to be emphasized is the fact that, whereas the primary cancer of the prostate is usually small, metastases from it are commonly extensive. The most frequent sites are the skeletal bones and the lymphatic glands. Visceral metastasis is comparatively infrequent, probably occurring in about 25 per cent. Kaufmann[12] remarks the infrequency of glandular metastasis from prostatic cancer compared with that from cancer of other structures. In 100 collected cases this author found involvement of the pelvic glands 27 times; iliac, 24; inguinal, 16. Young, whose figures agree with those of Kaufmann as to the involvement of the pelvic glands, says: "It shows the fact that one should not expect enlarged glands before making a diagnosis of carcinoma of the prostate." Blumer[13] states that cancer of the prostate gives rise to metastasis in bones in a much larger proportion of cases than any other form of cancer—probably in two-thirds of patients in whom it is allowed to run an unobstructed course. Von Recklinghausen[14] emphasizes the fact that the cancerous focus in the prostate is, in comparison with the advanced foci in the bone, small and in-

significant. The author directs attention to the analogy between metastasis in bone from a small nodule of cancer in the female breast and that from cancer of the prostate, and gives warning to suspect these sources in case of severe pain in the spinal column without evident cause. Blumer advises similarly in case of spastic paraplegia—involvement of the spine—and apparent osseous tumors in flat and long bones. In the thyroid, likewise, certain forms of malignant tumors occur which present entirely analogous relations, and such growths may be so small as to escape attention (von Eiselsberg[15]). The metastasis in bone is more or less general; its transmission is vascular rather than lymphatic, and nearly always originates in the medulla—rarely beneath the periosteum (Blumer).

SUMMARY

1. An analogy exists between the microscopic fields of epithelial changes observed in cancer of the prostate and those of the mammary gland, as presented by MacCarty.

2. In the undoubted histologic picture of cancer both organs present in the stroma migratory epithelial cells which are morphologically indistinguishable from the hyperplastic undifferentiated cells within the acinus.

3. According to the studies of MacCarty, these intra-acinic, hyperplastic, undifferentiated cells represent the precursors of the specific functional cells of the gland; consequently, the positively cancerous cells are the direct, immediate descendants of those which become the differentiated cells under normal conditions.

4. This analogy between the prostate and the mammary gland being accepted, further support is added to MacCarty's deductions, drawn from extensive studies of the breast; and, if adequately prolonged and comprehensive investigations in the future confirm the present view of the latter author, then it may be stated of prostatic cancer, as well as of cancer in general, that the process is fundamentally one of epithelial hyperplasia of the above-described undifferentiated cells, in a state of reaction to an abnormal irritant; furthermore, that for the pathogenesis of cancer it would not be necessary to assume the theory of "prenatal or postnatal rests."

5. Cancer of the prostate is a comparatively frequent disease after fifty years of age.

6. The process usually begins in the posterior lobe, and occurs more commonly as a small nodule or nodules of slow growth; consequently, *careful investigation of the posterior lobe, gross serial sections of the specimen, with microscopic examination of doubtful areas, are essential for diagnosis in the majority of cases.*

7. The fascial strata associated with the prostate seem to be quite effective barriers to the progress of the disease.

8. The tendency of extension of the cancerous process is upward to the region defined by the fascia of Dénonvilliers posteriorly, and the trigone anteriorly, and then beyond this area.

9. Metastasis affects bones, lymphatic glands, and internal organs. The cancerous focus in the prostate may be, and commonly is, insignificant, while the metastasis in bone is extensive. Similar relations have been observed with small cancerous nodules in the female breast and the thyroid. Manifestations in bone, with cause obscure, should direct attention to these observations.

10. Involvement of lymphatic glands is not a dependable factor in diagnosis, since metastasis may be present in the skeletal structure and these glands apparently unaffected.

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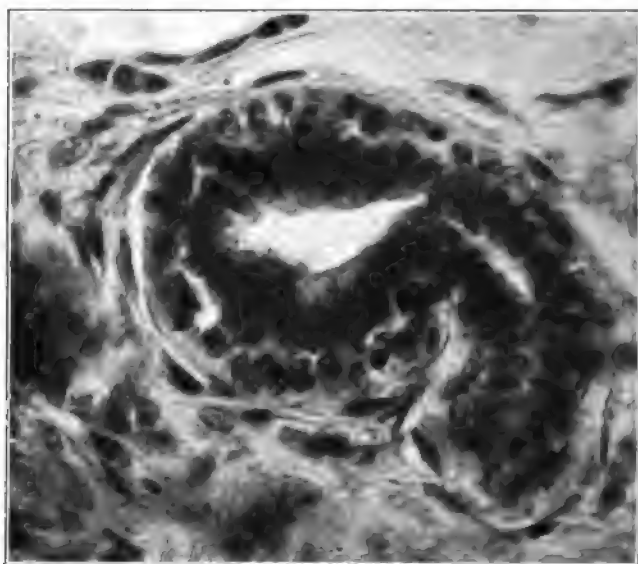
Fig. 313.—Breast; acinus showing primary epithelial hyperplasia (MacCarty).
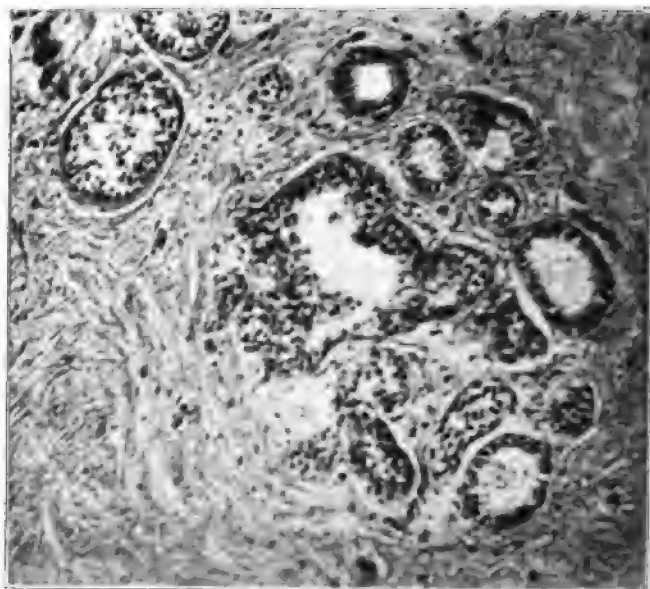
Fig 314.—Breast; acini showing secondary hyperplasia and confusion of line of demarcation between acinus and stroma (MacCarty).
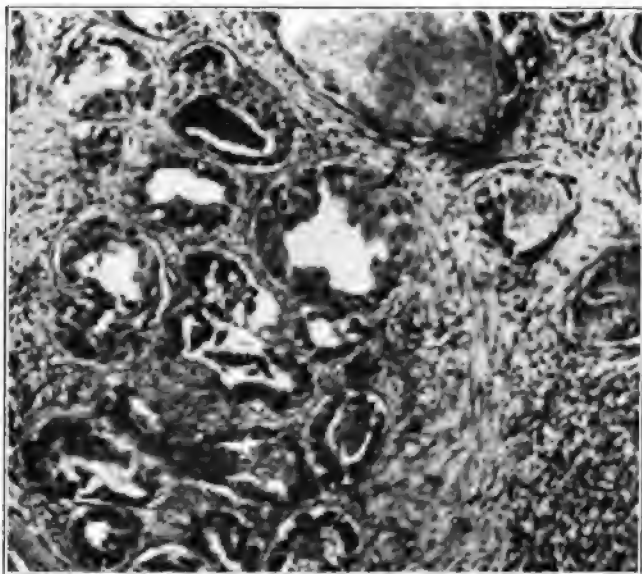
Fig. 315.—Breast; acini showing secondary epithelial hyperplasia (MacCarty).
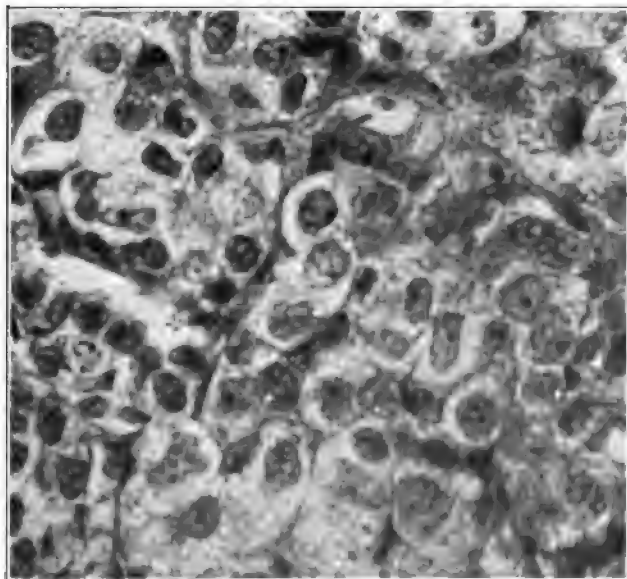
Fig. 316.—Breast; tertiary epithelial hyperplasia showing irregularities of nuclei—cancer (MacCarty).
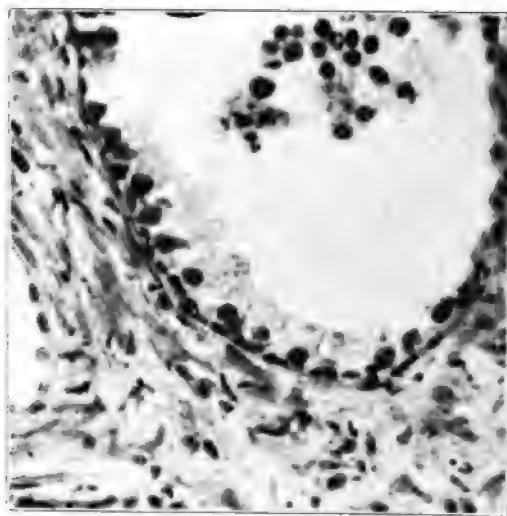
Fig. 317.—Normal prostatic epithelium.
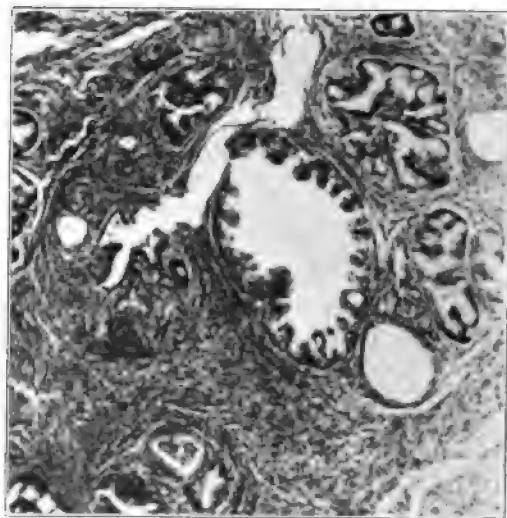
Fig. 318.—Normal prostatic epithelium, proliferating and projecting in masses in the lumen of the
acinus.
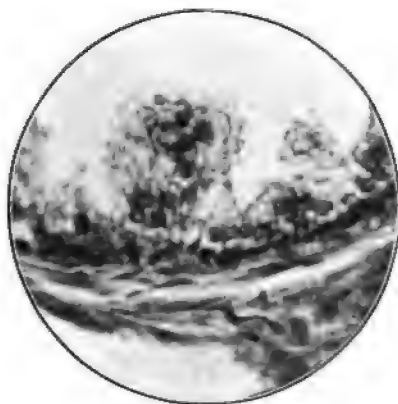
Fig. 319.—Normal prostatic epithelium, proliferating and projecting in masses in the lumen of the acinus.
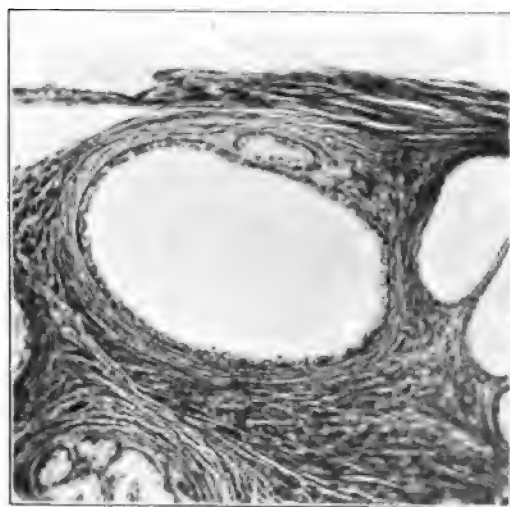
Fig. 320.—Cystic acini, showing two rows of cells, inner and outer row, similar to pictures seen in breast in primary hyperplasia.
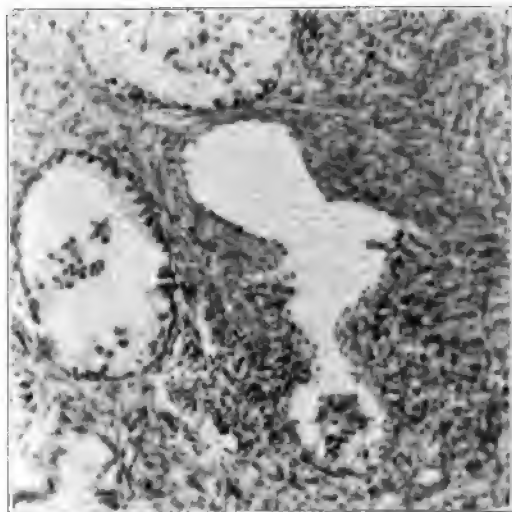
Fig. 321.—Normal epithelium in acinus, acinus with exfoliation of differentiated cells, acinus with some exfoliated differentiated cells and invasion (?) of stroma by hyperplastic cells of the outer row.
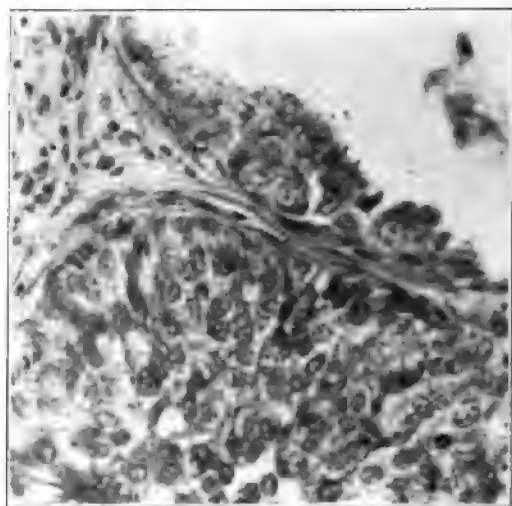
Fig 322.—Same as Fig. 270, showing in upper acinus primary and secondary hyperplasia; in lower acinus, secondary hyperplasia.
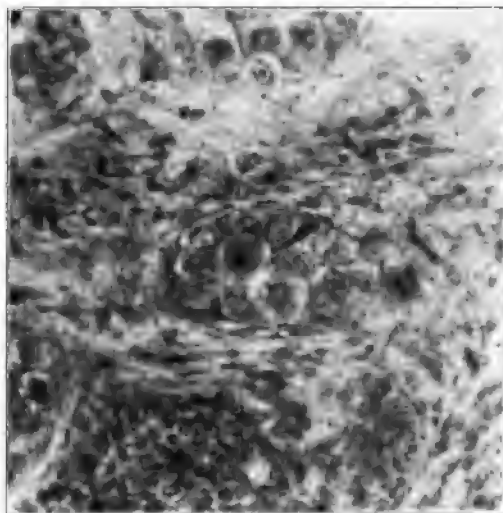
Fig. 323.—Same slide as Figs. 269, 270, 271, showing hyperplastic epithelial cells in the stroma, probably a lymphatic space (tertiary epithelial hyperplasia, or cancer). The cells are morphologically indistinguishable from the intra-acinic hyperplastic cells of the outer row (secondary hyperplasia).
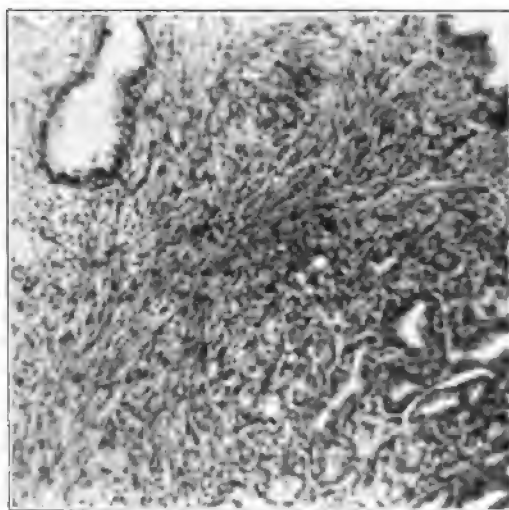
Fig. 324.—An apparently normal acinus above, to the right, and adenocarcinoma below, to the left, with fibrous band between.
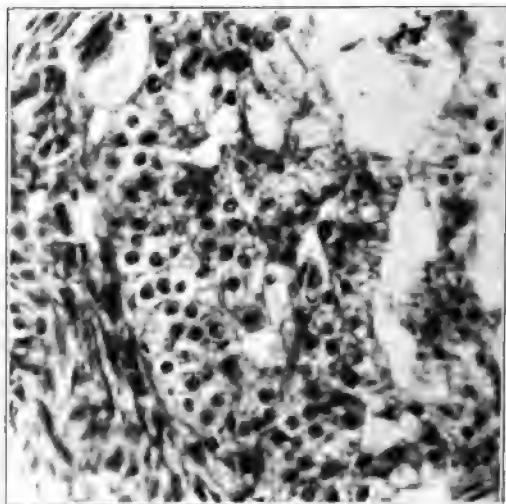
Fig. 325.—Tertiary hyperplasia—cancer.
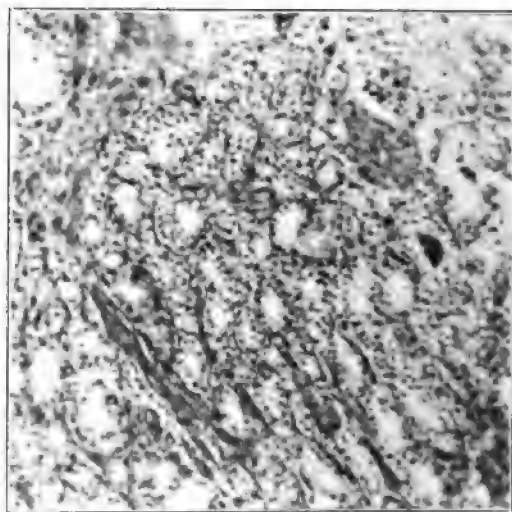
Fig. 326.—Adenocarcinoma.
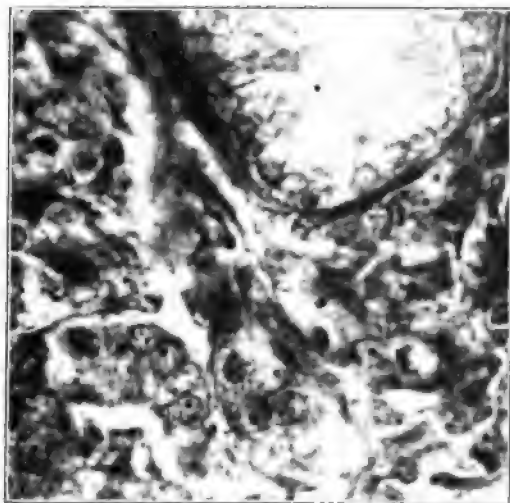
Fig. 327.—High power of adenocarcinoma.
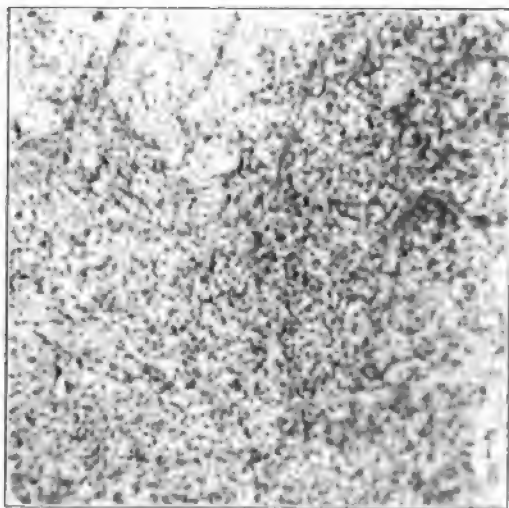
Fig. 328.—Medullary and diffuse carcinoma. See also Dr. MacCarty's Cancer Studies, Figs. 254, 287, 295, 296, 297, 298, 299, 300.

THE PROPHYLAXIS OF CANCER*

WILLIAM J. MAYO

All vertebrate animals suffer from cancer in situations which are affected by their habits or conditions of life leading to local lesions in the protective mechanism. We must, therefore, look upon local lesions as an invitation to cancer without regard to just what the actual cause of cancer may be.

If parasitic agencies are the cause of cancer, it would appear that their introduction into the human economy was affected through local lesions. The strongest evidence as to the parasitic nature of cancer and the best research on the problem with which I am acquainted is the work on the production of plant cancer by Erwin Smith,[1] which agrees in its main essentials with what we know about cancer as it exists in the human race.

On the other hand, if the cancerous process is one which is brought about by failure to restore normal conditions at the site of a local lesion by means of mature cells and the eventual calling forth of partially differentiated cells of an embryonic type in response to continued irritation, the rôle of the local lesion in either case is as important as is the actual cause.

It is probable that a large majority of human beings possess an immunity to cancer, that a lesser number possess a partial immunity, while a minority are without those protective agencies which render the local lesion ineffective. The term "precancerous," while not strictly accurate, has become allowable through custom and graphically describes a clinical condition, as pointed out by Rodman.[2]

The clinician can say with a great deal of assurance that a certain lesion is benign, that another is malignant, but there still exists a number of mid-ground lesions of which he is unable to say that they are either benign or malignant.

The pathologist, by microscopic examination, can, in a much higher percentage of cases, definitely establish the benignity or malignancy of a growth. But there occur certain growths which, even upon minute investigation, he will be unable to diagnose positively as benign or malignant. Sections from such growths sent to different pathologists may bring back contradictory opinions, the majority being undecided.

The microscopic picture which exists in these cases shows a change in character of the cells quite different from the normal, but as yet showing no invasion of the surrounding tissues.[3] This invasion is held by most pathologists to be essential in establishing malignancy. Pathologists, however, are striving to establish criteria whereby the change in the character of the cells may be shown to indicate malignancy before invasion takes place. Such microscopic appearance is found in the periphery of malignant growths and in chronic lesions which have been known later to develop malignancy. *The term "precancerous," therefore, strictly should not be applied to all local lesions which may be followed by cancer, but only to those local lesions in which cellular changes are taking place that surpass the normal attempt at repair of the lesion itself, but which are not as yet infiltrating surrounding tissue, the local lesion acting as the invitation, the precancerous stage as its probable acceptance.*

Sites of local irritation may be divided into three general groups:

(1) *Congenital* or acquired neoplasms, such as moles, warts, and benign tumors of various sorts which may undergo malignancy. Keen,[4] in 1904, called attention to the danger of degeneration of local lesions of this character and presented most interesting and instructive data in regard to their relation to cancer. Bloodgood,[5] in recent years, in a series of remarkable papers on the cancer problem, points out that, of 820 pathologically fully developed cancers of the skin and visible mucous membranes, he was

'14—42

unable to find a single case with a well-taken history which showed the absence of a previous defect which might be looked upon as a precancerous lesion.

(2) *Trauma.* Coley[6] calls attention to the influence of trauma not only in the development of sarcoma, which has been an accepted fact for a generation, but also to the fact that trauma has a strong influence in the production of carcinoma. Coley made an analysis of 250 cases of carcinoma which came under his personal observation and the histories of which were taken by himself. There was a history of antecedent trauma in 32.8 per cent. of the cases. The influence of trauma in the production of cancer has also been pointed out by McWilliams,[7] von Bergmann,[8] Röpke,[9] Murphy,[10] Ziegler,[11] Löwenthal,[12] Liebe,[13] von Graefe,[14] and others.

(3) *Chronic irritation,* whether the result of mechanical, chemical, or infectious agencies, is the most important of all those precancerous conditions with which we are acquainted, and it is undoubtedly the most potent influence in the development of the disease following congenital lesions and trauma. It is to be noted that cancer in any part of the body which is open to inspection may be shown, in practically every instance, to be preceded by a local lesion. The following well-attested examples may be cited: The development of cancer in the mouth from betel-nut irritation; the cancer of the groin in chimney-sweeps and sailors; the development of cancer following chemical irritation caused by tar, paraffin, petroleum, arsenic, and anilin products; the development of cancer in local lesions produced by heat, as cancer of the lip from smoking; the "kangri" sores following burns; those cancers on the shins of locomotive drivers who have been exposed for years to the direct action of heat; cancers following chronic irritation due to different forms of radiant energy, x-ray, etc.; cancers following the local lesions due to infections, such as bilharzia of the bladder, Treponema pallidum in keratosis linguæ;[15] nematodes in testicular tumors in horses[16] and in gastric cancer of rats;[17] and, rarely, the development of cancer in the glands of the neck as a result of the combined chemical and infective irritation of tuberculous cervical adenitis.[18]

A study of some particular forms of cancer which occur in great frequency as the result of a particular form of chronic irritation is most instructive. An interesting instance is the "horn-core" cancer of cattle, due to the irritation of the ropes through the horns with which the cattle pull their loads.[19] Even more extraordinary is the kangri-burn cancer on the abdomen, thigh, or vicinity, due to the hot kangri fire-baskets which the natives of Kashmir wear on the lower abdomen under the clothing in cold weather. Neve[20] states that, from 1890 to 1899, 2020 natives with tumors were operated on at the Kashmir Mission Hospital. Of these tumors, 496 were epithelial cancers, of which 363 were kangri-burn cancers. Equally striking is the betel-nut cancer of the mouth as seen in India. Neblock[21] states that, of 976 carcinomas treated in the Madras General Hospital from 1892 to 1901, 411, or nearly 50 per cent., were located in the mouth. Cancer of the lip is rarely seen except in smokers. Cancer of the groin is practically confined to the chimney-sweep and the sailor. Chinese men are subject to cancer of the posterior wall of the pharynx, due to the hot rice which they eat; the women eat at the second table when the rice is cold, and are not thus afflicted.

Can we doubt that if the kangri fire-basket were not worn by the natives of Kashmir that this strictly localized form of cancer would not exist? If the betel-nut were not used, the enormous preponderance of cancer of the mouth would not exist in India.

The prophylaxis of cancer on the visible portions of the body includes: the avoidance of all those habits and customs which have been shown capable of producing conditions favorable to the development of malignant disease; the removal of all congenital or acquired local lesions, such as Keen and Bloodgood have shown to be prolific forerunners of malignant degeneration; and the careful observation of patients for early evidences of malignant change following trauma.

Can our knowledge of the development of external cancer be applied to the solution of the problems of the development of internal cancer? Admitting that the mass of evidence as to the rôle of chronic irritation in its various forms and types is the most im-

portant factor in the development of cancer in the parts of the body which are exposed to the eye, must we not conclude that cancer on the inner surfaces of the body depends on the same precancerous conditions? It is difficult to find evidence as to the early appearance of cancer on the internal mucous surfaces of the body be-
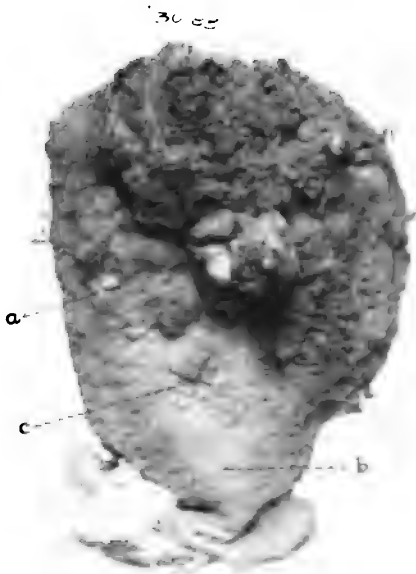
Fig. 329.—(Case 23026G (H30188).) Gross specimen, cancer of gall-bladder developing in mucosa long irritated by gall-stones: *a*, Cancer; *b*, normal mucosa; *c*, area in which mucosa has been eroded by gall-stones, non-cancerous.

cause, in the early stage, there are, as a rule, no manifestations which lead to a visual examination. Yet we have seen a very considerable number of such early cases and we have observed no instances of early cancer in the mucous membrane of the inner surfaces of the body which did not show the presence of a previous local lesion.

In nearly all the cases of cancer of the gall-bladder which we have had an opportunity to examine carefully gall-stones were

either present or there was evidence to show that they had been present (Fig. 329).[22]

One is impressed with the collateral evidence that the incidence of gall-stones and cancer of the gall-bladder shows the same increased frequency in the female over the male. Can we doubt that early removal of gall-stones might prevent cancer of the gall-bladder? The mortality of an early operation for gall-stones, other things being equal, is less than $\frac{1}{2}$ per cent. Cancer of the gall-bladder occurred in nearly 3 per cent. of all the cases of cholelithiasis which came to operation in our clinic. We have had no permanent cures after cholecystectomy for cancer of the gall-bladder which had been diagnosed as cancer previous to operation. A number of cures have followed the removal of early cancer incidental to the removal of thick-walled functionless gall-bladders, thus showing that it is not the nature or situation of the malignant process, but the delay in diagnosis, which is so fatal.

Cancer of the stomach forms nearly one-third of all the cancers of the human body. So far as I know this is not true of the lower animals nor of uncivilized man. Trustworthy evidence on this point is, for obvious reasons, difficult to obtain. Why is there this extraordinary frequency of cancer of the stomach? Is the stomach a trap and the cancer parasite, if it be a parasite, strained out in the stomach? If that were true, why should not cancer of the stomach be as frequent in the lower animals as in man? In rats, cancer of the stomach is exceedingly common when the animals feed on cockroaches infested with nematodes, which cause a chronic irritation of the rat's gastric mucosa.[17] Under other conditions it is very rare in these animals.

Whenever cancer is found with great frequency in certain situations or in only one class of individuals, it appears to depend on a single cause; this is probably true of gastric cancer. Is it not possible, therefore, that there is something in the habits of civilized man, in the cooking or other preparation of his food, which acts to produce the precancerous lesion? And it is probable that there is just one cause, since, if there were many causes, gastric cancer in man would have no such preponderance. Numerous

factors would cause the development of cancer in other races and species equally exposed to their action.   If we could but know what peculiar agency was responsible for the extraordinary frequency of cancer of the stomach the knowledge would play a great part in the prophylaxis of cancer.

Has the question of the acidity of the stomach anything to do with the problem?   The frequency of cancer in the stomach and in the large intestine, where the secretions are acid, and the absence of cancer in the small intestine, where the secretions are alkaline, is a remarkable fact.   Yet this acidity of the stomach is not confined to man, but, so far as I know, the extraordinary frequency of cancer of the stomach is confined to man and to civilized man. Further investigation is needed to elucidate this most interesting problem, and a possible source of information may lie in a comparative examination of the anatomy, physiology, and pathology, and, especially, of the habits of those races of man and those lower animals in whom cancer of the stomach is rare.

Among the precancerous lesions of the stomach, ulcer is the most common.   Yet it is a curious fact that ulcer of the duodenum is three times as frequent as of the stomach, though cancer of the duodenum is rare.   True it is, however, that ulcer or some other lesion in the stomach, which is of sufficient gravity to produce symptoms not necessarily of ulcer, but symptoms of chronic irritation, existed in more than half of all those cases of cancer of the stomach in which we have been able to make a resection, and in a high percentage of these an ulcer was found pathologically [23], [24] (Figs. 330 and 331).   Some pathologists believe that these ulcers are carcinomatous from the beginning.   If so, then the base of the ulcer should be carcinomatous (Fig. 332), but in our cases there was no cancer in the base of the ulcer—it was the overhanging margin of the ulcer which showed the cancer (Figs. 333 and 334).   It is evident that precancerous lesions exist in the stomach and that these lesions, while possibly not always ulcer, give clinical evidence of their presence in the precancerous stage in at least 50 per cent. of the cases in which the history is taken with this point in view. The extraordinary muscular activity of the stomach in the condi-
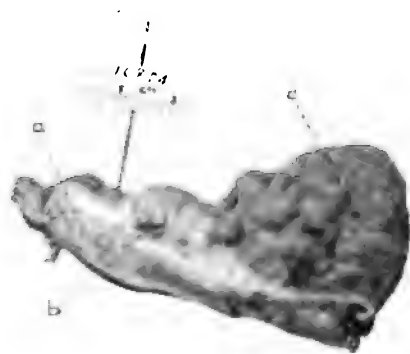
Fig. 330.—(Case 5705G (H16824).) Gross section through cancer of the pylorus; one of the very few cases in our series which did not show evidence of ulcer: *a*, Pylorus; *b*, cancer; *c*, normal gastric mucosa.
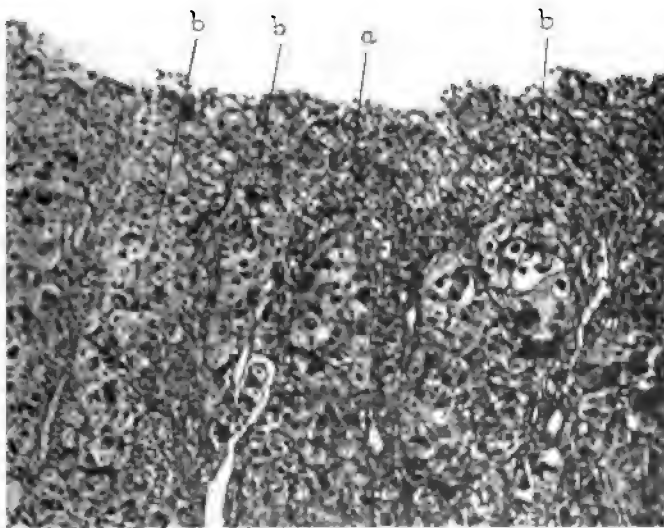
Fig. 331.—(Case 80107.) Microscopic section through base of ulcerated portion of gastric cancer: *a*, Granulation tissue; *b*, cancer-cells. In this specimen there is no pathologic evidence of ulcer preceding the cancer.

Fig. 332.—(Case 6838G (H18088).) Pyloric portion of stomach with multiple ulcers, two of which show areas of cancer within their borders: *a*, Pylorus; *b*, chronic ulcers; *c*, ulcers with cancer developing thereon.
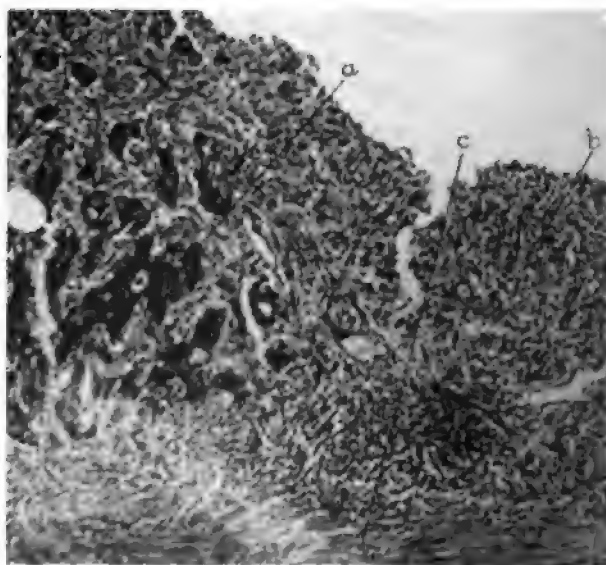
Fig. 333.—(Case 77369.) Microscopic section of margin of base of gastric ulcer showing cancer developing therein: *a*, Granulation tissue in border of ulcer; *b*, cancer-cells; *c*, scar tissue in base of ulcer. (Compare with Fig. 330.)

tion known as pylorospasm, which may result from gall-stones, duodenal ulcer, fecal stones in the appendix, or intestinal lesions, may account for the chronic gastric irritation in some cases. It is even possible that, through the influence of this great muscular contraction, cells may be loosened and even forced into the underlying tissue.

The prophylaxis of cancer of the stomach consists not only in the removal of gastric ulcers, but also in the relief of all those

Fig. 334.—(Case 1375GH.) Microscopic section of margin of base of gastric ulcer showing cancer developing therein: *a*, Granulation tissue in base of ulcer; *b*, scar tissue in border of ulcer; *c*, scar tissue in base of ulcer; *d*, cancer-cells.

conditions which cause gastric irritation resulting in the symptom inadequately and possibly incorrectly described as pylorospasm.

Cancer of the small intestine is extremely rare. In a series of 1882 cancers of the gastro-intestinal canal operated on in our clinic (October 1, 1897, to November 1, 1913), only 22 were cancers of the small intestine. Why is there this relative immunity of the small intestine over the stomach and the large intestine? The

small intestines are the most primitive part of that system on which the maintenance of the body-functions depend. Is it possible that in the long heredity of this particular part it has developed an immunity? There is something fascinating about this theory as accounting for the lack of immunity in the stomach and the large intestine, which have relatively a short heredity. The small intestine is exceedingly primitive. That the age of any part of the body has much to do with its ability to resist disease is
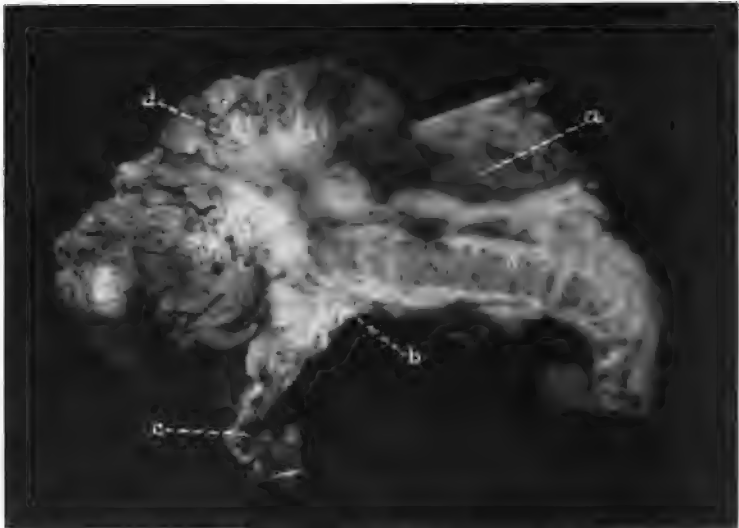
Fig. 335.—(Case 61097.) Gross section through pylorus showing cancer developing on a papilloma which springs from the duodenal side of the pylorus: *a*, Gastric mucosa; *b*, pylorus; *c*, duodenum; *d*, cancer.

well known. Though it may be a figure of speech that woman was formed from the rib of man, yet it is certainly true that the ovary is descended from the testicle and that the testicle is the primitive organ found in bisexual species.[25] Tumors of the testicle are rare. As shown by Ewing,[26] all the new-growths of the testicle with few exceptions are teratomas, the most primitive type of neoplasm. The ovary, on account of its short heredity, is subjected to a multitude of diseases and a large variety of tumors.

Beard's[27] theory that the immunity of the small intestine is due

to the pancreatic secretion destroying whatever malignant virus may exist therein may also be mentioned. It is interesting to note, however, that the small intestines have comparatively few sources of chronic irritation, and that when malignant disease of the small intestine is found, it is usually due to a preëxisting lesion, such as a degenerating polyp, adenoma, or papilloma (Fig. 335).

Cancer of the appendix usually occurs in association with chronic obliterative processes[28] (Fig. 336).

Fig. 336.—(Case 25398 (H31025).) Microscopic section through cancer in the tip of an appendix, the mucosa of which apparently had been obliterated by chronic inflammation: *a*, Cancer-cells; *b*, connective tissue.

The large intestine has a much greater liability to malignant disease than the small intestine, and the frequency with which cancer is found to be grafted on a source of chronic irritation must lead to the conclusion that the soil produced by chronic irritation needs only to be activated by the cancerous virus to produce cancer in susceptible individuals. The rule is that the original lesion, by the time operation is made, has been completely obscured

by the carcinomatous process, but in all our early operations lesions of a precancerous nature were found.   Especially is this true of the sigmoid and rectum, where, in 37 cases of diverticulitis, the irritation of the little hard balls of fecal material in the ends of these pouches has given rise to malignant disease in 20 per cent. of the total [29], [30], [31], [32] (Figs. 337, 338, 339, and 340).   It is probable that the supposed long duration of cancer of the large intestine, cases of
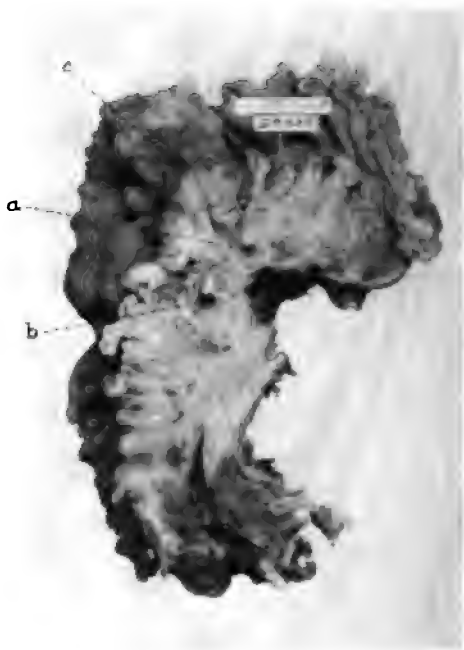
Fig. 337.—(Case 18633G (H28835).)   Gross longitudinal section through specimen removed from sigmoid showing chronic diverticulitis with cancer developing thereon: *a* and *b*, Diverticula; *c*, surface of cancer.

which have been reported, were in reality tumefactions from chronic diverticulitis, followed later by malignant change.

We must not lose sight of the fact that a changing physiology of an organ may be of itself a source of weakness and possibly act as a cause of local irritation.   Such a change is undoubtedly going on in the proximal half of the large intestine.   Plant life is parasitic
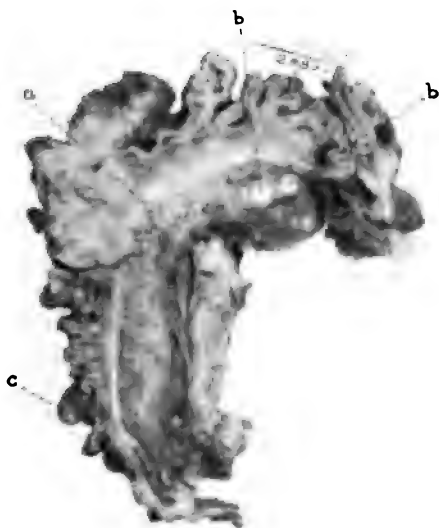
Fig. 338.—(Case 18633G (H28835).) Gross longitudinal section through same specimen as shown in Fig. 377 at level marked c, showing cancerous areas: a, Cancerous mass surrounding almost completely obliterated diverticulum; b, b, metastatic cancer of lymph-glands; c, normal mucosa.
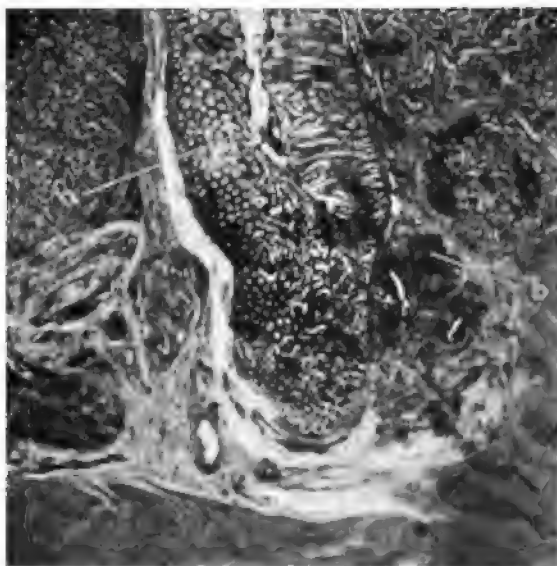
Fig. 339.—(Case 9496G.) Microscopic section longitudinally through a diverticulum of the sigmoid in the wall of which cancer has developed: a, Hyperplastic mucosa; b, cancer.
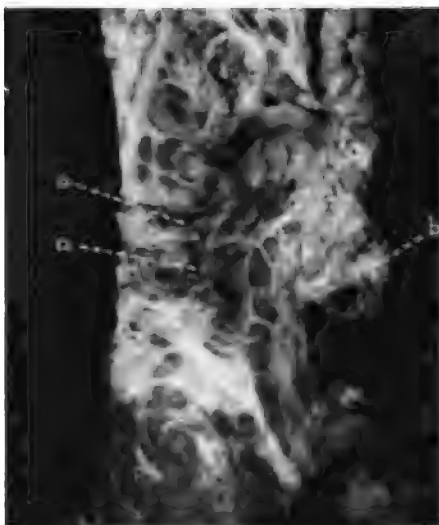
Fig. 340.—(Case 37405.) Gross longitudinal section through the wall of rectum showing diverticula around which cancer has developed: *a, a,* Diverticula; *b,* surface of cancer which, starting around the diverticula, has extended to the mucosa.

Fig. 341.—(Case 46337.) Uterus opened to show cancer beginning at point where endometrium has been chronically irritated by a fibroid in opposite wall of uterus: *a,* Cancer; *b,* fibroid; *c,* cervix; *d,* right tube.

on the inorganic world and depends on chlorophyl for its potency. We should know more about chlorophyl upon which, in the last analysis, life depends. Animal life is parasitic upon plant life, man on both plant and animal and increasing rapidly the flesh intake. Within the last one hundred years four times as much meat is taken as before that time.[33] If flesh foods are not fully broken up, decomposition results, and active poisons are thrown
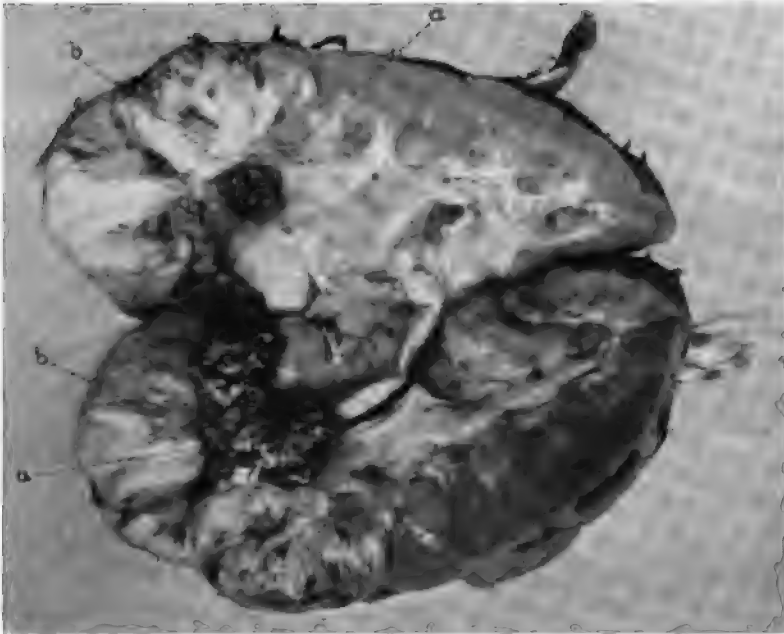
Fig. 342.—(Case 83255.) Gross section through kidney showing cancer developing in tissue chronically irritated by stones: *a, a,* Stones; *b, b,* cancerous areas.

into an organ not intended for their reception, and which has not had time to adapt itself to the new function.

The development of malignant disease in the uterus and kidney shows the same relation to chronic irritation. Cancer of the cervix occurs 15 times as frequently as cancer of the body of the uterus, but in myomatous disease cancer of the body of the uterus is found five times as frequently as cancer of the cervix, the chronic irri-

tation of the uterine tumors increasing the incidence 75 times (**Fig 341**).

Of all the cases of epithelial cancer of the kidney which came to operation in our clinic, not less than 50 per cent. were demonstrably superimposed on extensive renal calculus formation (**Figs. 342 and 343**).

In conclusion, I again call attention to the fact that preëxisting
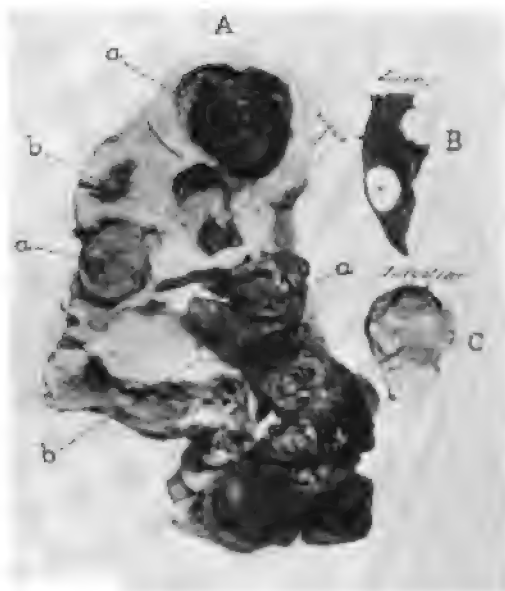
Fig. 343.—(Case 30265.)   *A*, Gross section through kidney removed at operation, showing cancer developing in tissue chronically irritated by large stones; *a, a*, stones; *b, b*, cancerous tissue; *B*, metastatic cancer in liver of same case (autopsy); *C*, metastatic cancer in wall of intestines from the same case (autopsy).

lesions play the most important part of the known factors which surround the development of cancer, that such precancerous lesions are produced by some habit or life condition which causes chronic irritation, that where cancer in the human being is frequent, a close study of the habits of civilized man as contrasted with primitive races and lower animals, where similar lesions are conspicuously rare, may be of value, and, finally, that the prophylaxis of

cancer depends, first, on a change in those cancer-producing habits and, second, on the early removal of all precancerous lesions and sources of chronic irritation.

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THE CANCER PROBLEM*

WILLIAM J. MAYO

Cancer in its inception is a local disease, and if removed at that time is curable. Let us, therefore, bend all our efforts toward the recognition of the disease while in the curable stage.

In Germany a cancer propaganda comparable to the tuberculosis work conducted in America has led to marvelous results. A much higher percentage of cancer victims reaches the surgeon in time for operation there than we are accustomed to see in our own country. It is estimated that, as a result of the tuberculosis campaign in the United States, 20,000 lives that were formerly sacrificed to the disease are now saved each year. The laity must be educated in regard to cancer as they are being educated regarding tuberculosis, and, fortunately, means have recently developed that will be exceedingly helpful in extending the educational influence of the medical profession in this respect.

The great majority of people believe cancer to be essentially an incurable malady. I venture to say that, if one were to go into the street and talk with ordinarily well-informed citizens, he would find the conviction among them that cancer was incurable, and the few which, in their personal observation, had been cured, were regarded as the exception and not the rule. This view, I am sorry to say, is shared by many medical practitioners of the older school. Why has the public become so confirmed in the belief that cancer is incurable, and how has this pessimism been fostered?

Heredity.—Perhaps one of the most unfortunate results of a logical inquiry into the influence of heredity on the causation of

cancer has been the encouragement of a belief that cancer is a hereditary disease, and therefore carries a stigma with it. The person who has been successfully operated on for cancer conceals the nature of his malady with the same solicitude he would probably conceal the fact that he had "done time" in a penitentiary. He does not wish his business world to know, as it would be looked upon as an obstacle to his career. Moreover, he does not wish his family to go through life thinking they are predisposed to this disease because he has had it. The result is that of the hundreds of patients who have had cancer and who have been cured by operative means, the public knows little or nothing, while those who have had cancer and been operated on without success are known to all. The community remembers only too well the suffering of the victim and the dreadful end. The subject is discussed throughout the neighborhood, and too frequently the operation is confused with the disease, prejudicing people against surgical relief.

Is there any justification for the view that cancer is hereditary? So far as I know there is no evidence that would lead to this belief. We know that overwork, worry, and bad nutrition, or what might be called general unhygienic conditions, will so affect the tissues of certain families as to break down their resistance to tubercle bacilli. It is possible that, in this sense, there may be families whose tissues, subjected to chronic irritation, may be more liable to develop the disease than the average individual. But even this is purely problematic and by no means proved.

I have often been told of instances in which members of the same family have suffered from cancer at about the same time, and these coincidences are held of great weight. Yet these combinations may arise at any time, just as a card-player may occasionally hold four aces or a royal flush; they are not due to chance, but depend on mathematical laws. This is equally true of "cancer houses" and "cancer towns." Always, when carefully investigated, the facts do not bear out the assertions. Small towns in older settled countries have more cancer than new towns—they have more people of a cancer age; the younger people have left for new fields.

The medical profession has done much to engender the belief in the heredity of cancer. The person supposed to be suffering from the disease is closely questioned regarding this point, and in such way as to lead him to believe that it is an exceedingly important fact. A good history should take heredity into consideration, but we should tell the patient and the family that, at the present time, there is absolutely no proof to warrant the belief that cancer is in any sense hereditary.

Hoffman, statistician of the Prudential Insurance Company of America, has carefully investigated the insurance mortuary records of this country, and denies that there is the slightest evidence presented in these enormous statistics to warrant the belief that heredity plays any part in the development of cancer.

Syphilis.—I have not seen over two dozen cases in which a good diagnostician would mistake syphilis for cancer. Yet the liability to this mistake has been dwelt upon and greatly magnified, and many individuals have advanced from the curable to the incurable stage while an effort was being made through antispecific treatment to eliminate the possibility. The patient perhaps presents himself with cancer of the rectum. His family physician dislikes to suggest to him a mutilating radical operation. He thinks over the cancers of the rectum that he has known to have been operated on and the record has probably been most unfortunate. The patients have been subjected to formidable operations, left with uncontrollable evacuations, and later have succumbed to the disease. The physician hopes against hope that it may be syphilis. He knows that it is often impossible to obtain a history of syphilis, or that it may have been accidentally acquired. The patient is in the early stage of cancer,—quite curable,—but since he has only a small focus of disease, it would be a terrible thing to subject him to a mutilating operation. Therefore the physician advises a prolonged course of antisyphilitic treatment. He eventually is confronted by the fact that it is not syphilis, and, in the mean time, the patient has passed from the curable to the incurable stage. Operation is then advised and is done, with the usual result.

The Wassermann reaction has, fortunately, come to our aid

and to the patient's rescue. It is no longer legitimate to subject a patient to a prolonged course of diagnostic antisyphilitic treatment. We should know at once whether or not it is syphilis, and in this way "may be it is syphilis" will not have the disastrous effect it has had in the past.

Not Lack of Knowledge, but Lack of Examination.—Mistakes in diagnosis from lack of careful examination is the most common cause of failure to recognize malignant disease in time for a curable operation. Many diagnosticians make one or two physical examinations but fail to continue to make them. If we are to protect our patients from misfortune, such examinations must be repeated as long as we have charge of the case. Who has not had the humiliation of having the patient first call his attention to a tumor that had developed sufficiently to be palpable since the last examination? The development of asepsis has brought about an aseptic conscience. The examining physician often hesitates to make the necessary examination because it involves soiling the finger. This is especially true of the rectum. Fifteen per cent. of the patients who come to us with cancer of the rectum have been recently operated on for hemorrhoids or treated for stricture. It is true that the patients had one or both of these conditions, but they also had a cancerous growth, and in each one of these patients the growth was in easy reach of the examining finger and could have been recognized by the sense of touch alone. How easy it is to carry a few thin finger-cots in the pocket so that such an examination can be aseptically carried out. The very presence of cots in the pocket suggests their use.

Inefficient Operations.—In this connection I come to a delicate subject, but one which I feel should be touched upon. There is too high a percentage of patients with cancer subjected to inefficient operation by inexperienced men. Because the disease is early, it appears as though it might be easily cured, and men who would not for one instant think of operating where a radical operation was to be done will often make a small operation—futile and hopeless— and thus sacrifice the life of their patient, because it is in this early curable stage that the operation should be most carefully carried out.

The surgeon has had a great share in creating the feeling of hopelessness which exists among the laity, and has often discouraged the general practitioner by his unwarranted attempts at radical procedures in plainly incurable disease or extensive palliative operations which fail to palliate. We have all witnessed extensive radical operations for hopeless cancer and, after a terrific and futile operation had been completed, heard the surgeon say, "Oh, well, it was hopeless anyway." But does that justify us? I am sure that, if surgeons were never to make another palliative operation for cancer, thousands of lives would be saved that are now lost through delay. The laity knows that such a patient was operated on, that he died a horrible death, but it does not know that the operation was a palliative one, and it confuses in its mind the last stages of the disease with all its sufferings with the operation rather than with the disease. Far better that the patient go home and tell the family and friends that it is too late for operation; then the suffering and death leave no such confusion in the minds of the people of the neighborhood. They see just what the disease has done, and from that neighborhood patients will come early, in contradistinction to the hopeless patients with inoperable disease who drift in from communities where too late or palliative operations have been the practice.

Do not understand me as saying that palliative operations should not be done. It is our duty to look after the individual and to do our best for him, but before we do a palliative operation, and especially before we do a mutilating operation, let us answer this question: "Will the palliation which the patient receives be worth to him the pain, the detention from his family, and the expense?" Or, better yet, let us bring it home and say to ourselves: "Would I allow one of my family to be subjected to this formidable operation with such slight prospects of cure or alleviation?"

Non-operative Methods.—If late and palliative operations for cancer promise so little, have we any other recourse to relieve such patients? In this connection I have been interested in investigating the results achieved by radioactive substances—x-ray, meso-

thorium, and especially radium—in the cure or palliation of cancer. I have talked with many men of experience in the great clinics, and few have exhibited faith in the curative properties of these agents in deep-seated or advanced growths, although all have seen superficial growths cured. It is evident that radioactive substances have a greater influence in sarcoma than in carcinoma, but, strange to say, few cases of sarcoma have been reported in which the cure has lasted as long as four years. It would seem, therefore, that these agents were capable of curing permanently small superficial carcinomas and of causing to disappear about 30 per cent. of sarcomas. As palliation is often marked and of long duration, and the use of radioactive substances subjects the patient to little discomfort, the field of application in such cases is broad. *But these agents should not be used in early growths curable by operation!*

The use of heat in cancer is an ancient practice. Ordinarily applied as a destructive agent by actual cautery, it is the only non-operative means which has stood the test of time. We are indebted to Percy for a scientific exposition of the value of heat, demonstrated both experimentally and clinically. He uses an electrocautery with a controlling rheostat, and operates through specula lined with chambers for the continuous flow of cold water to limit the application. Many observers have shown that the embryonic cell, such as the cancer-cell, has less vitality than the mature normal cell, and is especially affected injuriously by heat. The actual difference between the cancer-cell and the normal cell in ability to withstand heat has not been determined, but is probably from 15° to 30°. Percy demonstrated that heat could be made to penetrate deeply into the cancerous tissues, exerting a selective action by keeping in the range of this marginal difference. The cautery kills both the normal and the diseased cells, and in so doing develops a charcoal core which insulates the tissues against heat as though it were asbestos. Heat should be used, therefore, not as a cautery, but raised to such a degree as to coagulate the embryonic cells, and this effect, by a slow cooking process, may be made to reach out into the tissues, destroying the embryonic cells, far in advance of its effect

on the normal tissues. It is the scientific application carried to its logical conclusion of the only agent besides the knife that has retained its reputation throughout the history of medicine. So far as our experience goes, this method, applicable to a large variety of carcinomas in various situations, forms a palliation with prospect of cure in a group of cases in which the knife has been inefficient.

Improved Methods of Diagnosis.—How fortunate it is that there have recently been such additions to our diagnostic methods! The roentgenogram has added enormously to our ability to see into the hidden places of the body. This remarkable agent must be classed with macroscopic pathology as developed by John Hunter, with the development of the natural sciences due to the work of Darwin and Wallace, and with the germ origin of disease as advanced by Pasteur and Lister. Roentgen's work has reformed diagnostic methods, it has replaced speculation with facts, and yet we are only in the daguerreotype stage of x-ray photography. By this means we are now able to determine the nature of many obscure diseases of the digestive tract. For instance, in cancer of the stomach we can make an early diagnosis in 93 per cent. of the cases largely by the x-ray.

It is true that we had, in the exploratory incision, a means of fairly exact diagnosis in such cases, but this procedure carried with it a dread to the patient of an unnecessary operation, and too frequently developed the fact that it was too late for operation. The roentgenogram, therefore, gives us knowledge of the early case, so that we may operate with a prospect of cure and may also save the patient the distress of an unnecessary exploration and ourselves the humiliation of making it.

The results of operations for malignant disease have enormously improved within the last ten years, and much of this improvement must be credited to the clinical pathologist. Where we formerly worked under the influence of the eye and hand, we are now working under the influence of the microscope. The *frozen section* enables us to see the innermost nature of the diseased tissue during the progress of the operation, while the knowledge is of the greatest value to the patient. The development of diagnosis by means of

the frozen section has been somewhat slow. The pathologist, trained in the preceding generation, had learned to recognize certain artefacts in the tissues and to feel lost unless he found them. There is as much difference between the living tissues studied in the immediate frozen section and the tissues studied after several days of preparation as between surgery on the living and dissection on the cadaver.

It has been necessary to develop an entirely new technic and understanding of living microscopic pathology comparable to what we have experienced regarding the development of gross pathology of the living as contrasted with postmortem pathology. I often hear clinical men say that they would rather trust to their clinical experience than to the microscope. If it be true, I would I had their knowledge. I can only say that, of all aids toward improving the actual results of operation, none has been of more value to me than the frozen section.

Prophylaxis of Cancer.—Taking all things into consideration, I think we may look upon the future of the cancer problem with hope. We are advancing rapidly in our ability to recognize the nature of the process early, and we see the lines of progress distinctly.

We do not as yet know the actual cause of cancer, but we do know that it has its soil in a disturbance of the protective mechanism, usually of the skin or the mucous membrane of the body. And this is as true of cancer in the lower animals as in man, as previously stated. * * * *

Coöperation of the public is essential if we are to have the full benefit of our present knowledge. To say to laymen that cancer is curable in the early stage is not sufficient. They have no knowledge of what constitutes the early stage. Is it possible for us to teach them the nature of those influences which we know by experience may lead to the development of cancer, and if so, should they be taught *prophylaxis* as well as those indications which show that the disease has developed? No one has yet seen a cancer of the skin or visible mucous membrane of the body which was not pre-

*Mayo, W. J.: "Prophylaxis of Cancer," p. 659.

ceded by some form of chronic irritation. Investigation of the inner surfaces of the body reveals the same conditions always preceding cancer. Let us, therefore, say to the public: "Go to your physician at once on the discovery of any sign or symptom of irritation about warts, moles, and benign tumors or ulcerations, chronic inflammatory processes, or injuries however slight which fail to heal promptly."

When the laity understand that all sources of chronic irritation carry with them a deadly significance, the prevention of cancer will have been greatly advanced and the percentage of curable cases which come to the only known cure—operation—will be enormously increased.

THE SEPTIC FACTOR IN THE THREE PLAGUES*

WILLIAM J. MAYO

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The three plagues, syphilis, tuberculosis, and cancer, are the most wide-spread affecting the human race to-day. In each of these sepsis plays a most important part. In syphilis it is so important a factor that, unless it exists, we may not recognize the process as syphilis. In tuberculosis it is almost an axiom that people do not die from tuberculosis, but from the associated sepsis. In cancer sepsis renders many cases inoperable; it is the most important factor in the production of the painful and offensive results of advanced disease and the usual cause of death following radical operations.

SYPHILIS

"Unto the second and third generation"—how fitly this old quotation describes syphilis, and in this respect it is quite unlike tuberculosis and cancer, neither of which is transmissible in utero. The discovery of the Spirochæta pallida of syphilis and the newer methods of staining it have placed in our hands a great weapon of defense against this plague. Aided by the Wassermann reaction and salvarsan, we are for the first time in a position to combat the disease effectively.

It is believed by many syphilographers that syphilis in this generation is becoming milder as compared with the disease in former generations. Two reasons have been advanced for this: one, that the people are gradually developing an immunity by virtue of hereditary and acquired protective agencies, based on the

general theory of the survival of the fittest, and, second, that syphilis is much better treated now than it used to be. But how can we account for the high percentage of people with terminal changes in the central nervous system—tabes and paresis? Certainly there is no diminution of these syphilitic manifestations, making all due allowance for better diagnosis. On the contrary, they appear to be on the increase—the clinical frequency of locomotor ataxia and general paralysis of the insane is appalling.

The hardness in the base of the typical chancre and the accentuation of secondary lesions are not due to the spirochæte alone, but to complicating sepsis (Corner). The people of all civilized countries are far cleaner now than they used to be, and through improved hygienic knowledge take better care of small sores and abrasions than was formerly the custom. The chancre, therefore, is apt to be treated with strict cleanliness and often by antiseptic substances, so that it may not assume that typical hardness in the base which is due to sepsis. The failure to develop this characteristic because of the cleanliness and care of the individual may cause a failure to diagnose syphilis. For this same reason the secondary symptoms may be exceedingly mild, and thus the patient may acquire the disease and pass through the primary and secondary stages without detection. The tendency of the infection is to travel along the nerve-sheaths into the central nervous system, and the first symptom of syphilis known to the patient may be premonitory of tabes or paresis, terminal conditions for which the resources of our art have comparatively little remedy.

It is a great misfortune that syphilis is considered only a venereal disease, therefore carrying a stigma with it. As a matter of fact, a high percentage of the patients that we see with syphilis have had an extragenital source of infection. Lips, fingers, and abrasions at different parts of the body have been the means of communication. The failure to elicit a venereal history has frequently thrown the diagnostician off his guard.

We see a few cases every year of surgeons who have infected their fingers with syphilis during operations on syphilitic patients. The chancre often does not develop the typical characteristics

because of the care the surgeon naturally gives to minor abrasions, and, as his personal hygiene is good, he may slip through the secondary stage with scarcely a suspicion. Then come visceral lesions or lesions of the central nervous system. Occasionally, however, exactly the opposite condition prevails. The surgeon acquires syphilis and virulent septic infection at the same time, and here the syphilitic infection is masked by the septic involvement, which, however, does not prevent the eventual development of syphilis, which remains grafted on the individual after the septic manifestations have disappeared. If these accidents happen to the surgeon unrecognized, how much more liable is the ordinary individual to the same misfortune.

The importance of early diagnosis of chancre cannot be overestimated. Systemic infection does not take place until from five to fifteen days after the development of the chancre. At this time the disease is local, and by proper treatment can be cured. After the Wassermann reaction has developed the great opportunity has passed, for syphilis has become systemic. Prolonged treatment may or may not eventuate in a cure. This brings up the very important consideration that the spirochæta exist in the chancre and can there be readily secured for microscopic examination. *The diagnosis of chancre should depend on finding the spirochæte, not on the induration of the base.* Every suspicious infection should, therefore, be subjected to careful bacteriologic investigation, otherwise the patient may suffer irreparable damage.

Hale White gives the following table of the relation of syphilis to the general death-rate, showing that even in those cases which have been subjected to two years' treatment the death-rate by decades is nearly twice as high, to say nothing of the miseries and horrors of a loathsome disease:

CLASS 1.—SYPHILIS CERTAIN, THOROUGHLY TREATED; TWO YEARS' CONTINUOUS
TREATMENT AND ONE YEAR'S FREEDOM FROM SYMPTOMS

	ACTUAL DEATHS	EXPECTED DEATHS	RATIO, PER CENT.
Certain syphilis between three and five years prior to application	13	9.32	139
Between five and ten years	34	19.56	174
More than ten years	53	24.42	217

CLASS 2.—NOT THOROUGHLY TREATED OR NO DETAILS GIVEN

	ACTUAL DEATHS	EXPECTED DEATHS	RATIO, PER CENT.
Certain syphilis between two and five years prior to application...................	44	15.52	284
Between five and ten years	54	25.52	212
More than ten years....................	76	59.09	129

CLASS 3.—DOUBTFUL SYPHILIS

	ACTUAL DEATHS	EXPECTED DEATHS	RATIO, PER CENT.
More than two years prior to application	67	48.71	138

It is a curious fact that terminal syphilis in man affects the nervous system more frequently than in woman, and often pursues a more malignant course. In woman, as a satanic equivalent, syphilis is the great abortionist, and carries dreadful misfortune to the children she may bear, even unto the second and third generations. In certain situations syphilis leads to chronic irritation and cancer, as in the keratosis linguæ preceding cancer of the mouth (Blair), especially in smokers. It is well known that the tuberculous bear syphilis badly, while the syphilitic are prone to tuberculosis.

There is much food for reflection in the septic factor in syphilis. Those acquiring the disease accidentally and extragenitally will probably at the present time not have the chancre recognized, and the cleaner the person affected, the less chance that it will be recognized in the secondary stage. Those venereally affected and dirty have the best chance of early detection and prevention of systemic infection, and, if systemic infection does take place, by reason of the virulence of the secondary stage, to have it detected at this time and to secure thorough and adequate treatment.

It will take the profession a long time to rid itself of impressions of the disease which have been inherited from experience with the vicious and dirty, in which the prominence of the symptoms was due less to syphilis than to associated sepsis. Corner says: "At hospitals students are taught to recognize syphilis from the examples of septic syphilis brought to their notice by their teachers. The septic factor in syphilis exaggerates its characters and furnishes some new ones of so great importance that the great text-books have taken such septic characteristics as illustrative of the syphilitic nature of the lesion." As a corollary to this, Corner further says: "There are few diseases which, if recognized early, are more

studiously treated and more uniformly yield good results from treatment than syphilis." And, again, patients with "syphilis which is not recognized, and not treated, may transmit both to this and future generations. They then appear with nervous diseases, such as locomotor ataxia, general paralysis of the insane, and other forms of insanity, and there is no history of syphilis." I would emphasize Corner's final remark, that "if the patient belongs to the better educated classes he may pay a penalty for his cleanliness in the disease not being diagnosed, and the virtue which he undoubtedly has is not rewarded properly."

In abdominal surgery we unexpectedly meet with visceral syphilis, most commonly of the liver or stomach, and most of those cases are diagnosed as cancer. For this reason, when in doubt, a piece of tissue should be secured for microscopic examination of the frozen section and, while this may not definitely determine that it is syphilis, it at least will show that it is not cancer.

In regard to treatment: In the army, syphilis among the soldiers has been very largely prevented by the use of a 50 per cent. calomel ointment ($\frac{1}{4}$ lanolin and $\frac{3}{4}$ vaselin or lard), which was first used in the French army. It was found experimentally and clinically by Metchnikoff that if applied within five or six hours after infection, prevention was absolute. Suspicious sores should be subjected to examination for the spirochæte, and if present with a negative Wassermann reaction, the disease should be treated as a local one by the direct application of salvarsan emulsion or calomel ointment, and one or two preventive salvarsan injections made. It must be borne in mind in the treatment of lues as a localized infection that some cases become constitutional before the disappearance of the primary sore. For this reason a Wassermann test should be made at intervals and the patient watched for signs of constitutional infection.

Many instances of the failure of salvarsan to cure syphilis are recorded, with eventual cure by means of mercury, especially mercurial inunction. As a matter of fact, arsenic in one form or another has at various times in the history of medicine been heralded as a

cure for syphilis, but always has it eventually been shown to be inferior to mercury.

The value of the Wassermann reaction is very great, but in few serologic tests is the personal equation so prominent a factor. Blood drawn at the same time and sent to several serologists may lead to different opinions, but in our experience a strong positive Wassermann, made by a competent man, is fairly certain. However, before subjecting the patient to prolonged treatment, this test should be confirmed by a second and third examination. Unfortunately, a negative finding has little value. Syphilis may be present without a positive Wassermann reaction, especially if the patient has been recently treated.

TUBERCULOSIS

It is almost axiomatic that those afflicted with tuberculosis do not die from the disease, but from the associated sepsis. The chief exception is in tuberculous meningitis, where the products of bacterial action are confined in a bony box and produce pressure. The influence of sepsis on tuberculosis is most pernicious. In preantiseptic times the opening of tuberculous abscesses—so-called cold abscesses—was looked upon with great disfavor. It was well understood that incision into such an abscess was promptly followed by what was known as hectic, picket-fence temperature, and general physical loss to the patient in every way. The older writers called attention to the fact that, when a cold abscess opened spontaneously, it did not give rise to hectic, but that hectic always followed an incision, nature evidently contriving some valvular method of drainage which permitted the escape of the contents without admitting pyogenic organisms, a method which the surgeon could not imitate. It is true to-day that, no matter how careful the after-treatment may be, the incision and drainage of such an abscess are practically always followed by septic complications. It was for this reason that cold abscesses were aspirated and, after removing as much as possible of their contents, the opening was sealed. This is good practice at the present time. In many cases iodoform emulsion or formalin and glycerin was injected, hoping to

sterilize the cavity. To-day such abscesses, under strict aseptic precautions, are often opened by a free incision, thoroughly cleared out, and then filled with salt solution or mopped out with iodoform and glycerin, tincture of iodin, or glycerin and formalin, and sutured completely. These operations, however, have very little to commend them over simple aspiration, which was the early practice. Such abscesses, as a rule, have their origin in bony tuberculous lesions, although they may be seen in other situations.

Modern methods of treatment by rest and mechanical supports have greatly reduced the number of tuberculous abscesses, and the aspiration of those which form has reduced very materially the number of cases in which such abscesses open spontaneously with sinus formation. In the earlier time patients with tuberculous sinuses were very common, often maintaining a fair degree of health for years. One of the most pernicious practices was to probe such a sinus. This probing was almost invariably followed by septic infection. Fortunately, the practice has now become obsolete: such sinuses can be injected with Beck's paste and a roentgenogram taken which will show their ramification far better than probing. It should be remembered that, in the use of Beck's paste, asepsis should be carried out, since tuberculous sinuses the result of spontaneous opening of tuberculous abscesses are practically free from sepsis, and if infection is introduced into the sinus, sepsis with all its complications may follow and interfere with such prospect of cure or amelioration as might otherwise be derived from the Beck procedure.

The behavior of tuberculosis in the peritoneal cavity is greatly influenced by the presence and degree of sepsis. Tuberculous peritonitis is secondary to a local lesion usually in the Fallopian tubes or intestinal tract, or from retroperitoneal glands. Pure tuberculous infection of the peritoneum will seldom cause extensive adhesions. This variety is most often seen in connection with tuberculosis of the Fallopian tubes. It should not be forgotten that tuberculous peritonitis is a symptom and not a primary disease. It is in reality a conservative process. The abdominal ostia of the Fallopian tubes in tuberculosis are usually open, unlike

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gonorrhea, in which the fimbriated extremities of the tubes are nearly always closed (Murphy).

The products of tuberculosis of the mucous membranes of the tubes pass out through the open abdominal ends into the peritoneal cavity. The peritoneum promptly undertakes to remove these tuberculous products, and the resulting reaction, with the accumulation of ascitic fluid, we speak of as tuberculous peritonitis. It has been known for a long time that if the ends of the Fallopian tubes were open, free fluid and tuberculous peritonitis would exist, while if the tubes were closed there would be no tuberculous peritonitis, but the material would be retained within the tube, forming tuberculous pus-tubes, sometimes of huge size, containing typical tuberculous whey-like fluid. The ovaries are not often involved in this process to a greater extent than the intestines or the peri-· toneum generally. The proper treatment, therefore, is the removal of the tuberculous tubes, leaving the uterus and ovaries, and closure without drainage.

If drainage is used, we may have the development of sinuses, often followed by mixed infection from some intestinal focus, and finally, in many instances, by prolonged suppuration or fecal fistulas. The sequence is about as follows: When the drain is used, a certain amount of fluid escapes during the early period. After a few days the drain is removed and there is a little discharge. During the next week or two there is a constantly increasing discharge, which becomes purulent, and in the course of a month or six weeks a fecal fistula may develop from which a little gas and feces escape, troubling the patient for months or years. In some instances wide intestinal openings occur, with extensive septic infection of the already existent tuberculous lesions, and the patient dies. The drain has permitted subsequent infection.

It is very essential, therefore, that in tuberculosis of the peritoneum drainage should not be used *unless mixed infection is already present*. The old idea that tuberculous peritonitis could be cured by drawing off the fluids and that some special influence was created by exposing the peritoneum to air or by pouring in glycerin, iodoform, oxygen, or what not, was based on a misconception. It

is true that if the fluids were drawn off with a trocar cure did not result, and it is also true that if the abdomen was opened cure often did result, whether or not any other special treatment was employed.   This was due to the fact that when the abdomen was opened the fluid was thoroughly removed and the ends of the Fallopian tubes, which were separated from the surrounding parts because of the fluid, had an opportunity to become adherent to some neighboring point on the peritoneum, and the tubes, closed by those adhesions, no longer drained the tuberculous débris into the peritoneal cavity.   This tubal retention could often be detected by the gradual development of tuberculous pus-tubes after the ascites had disappeared.   Such tuberculous pus-tubes in the course of time may heal, but they usually remain a grave source of danger of general systemic tuberculosis.

Vaginal section was at one time very popular for pelvic infections—justly so for those phlegmons due to ordinary pyogenic organisms, such as occur postpuerperal or post-abortive.   The draining of a pelvic tuberculous infection from tuberculous tubes by an incision through the vagina causes most serious after-effects, and often a patient loses her life, not at once, but later through mixed infection and prolonged septicemia with multiple rectal and intestinal fistulas.

It can be laid down as a rule that pure products of tuberculosis in the pelvis should not be drained because of the impossibility of preventing septic complications.   They should be removed by a clean, careful operation through the abdomen without permitting septic infection and without permitting the chance of sepsis later from drainage.   Tuberculosis of the Fallopian tubes practically always involves both tubes.   This is also true of gonorrheal salpingitis.

I have given these few examples of the influence of septic complications as introduced by drainage which is quite parallel to the knowledge of the ancients in regard to the treatment of the cold abscess, showing the pernicious effect of drainage in permitting a subsequent mixed infection of tuberculous lesions.

Tuberculosis of the peritoneum, however, having its origin in

the intestine, is very liable to be a mixed infection from the start, and is peculiar in the fact that, instead of developing large quantities of fluid, it produces a distended abdomen filled with adhesions. Some of these greatly distended abdomens feel almost wooden on palpation, and on attempting to open the peritoneal cavity it will be found to be almost completely obliterated by adherent coils of intestine. There were many descriptive terms for this condition according to the extent and virulence of the complicating sepsis, from the completely adherent type, in which no free cavity of the peritoneum would be found below the transverse colon, and those milder and attenuated types in which free fluid would be found with comparatively few adhesions. This very interesting condition was long a puzzle, but I have been able to secure three cases in so early a stage that we found colon and other bacteria in connection with the tuberculosis. A little later the septic infection could not have been deterred because these bacteria, having a shorter life, would have been destroyed, and in the later stages only the tuberculous condition would have been apparent, although the adhesive process had been caused by the septic complication.

It is curious that the appendix, which contains lymphoid tissue analogous to the tonsil, is seldom the primary seat of tuberculosis. In the examination of 12,003 appendices we found tuberculosis in but 71 cases.

The effect of sepsis upon tuberculosis is well shown in the so-called hypertrophic tuberculosis of the cecum. Here a huge tumor may exist, with enormous thickening in the submucosa, giving a picture, almost typical to the naked eye, of carcinoma. Some cases of this kind have been opened up, believed to be carcinoma, and on account of the enlarged glands, usually from sepsis, however, rather than from tuberculosis, have been considered inoperable and a colostomy done. Such patients may live for years— supposed examples of the slow course of carcinoma of the cecum.

The ulcerative type of tuberculosis of the cecum under the influence of septic infection often forms fistulous communications between the cecum and the surfaces of the body which are most difficult to cure.

In 1899 I published an article on "Localized Tuberculosis of the Intestine." At that time it was not believed that primary localized tuberculosis limited to any portion of the intestinal tract ever occurred, but that it was always the result of pulmonary tuberculosis, usually from swallowed sputum. I called attention at that time to the fact that, in my opinion, cow's milk was responsible for this infection. I instanced that in the country districts pulmonary tuberculosis was comparatively rare, but that localized tuberculosis—of bones, joints, intestines, and glands—was exceedingly common; that it was customary to use raw milk as a regular article of diet, and that a considerable percentage of milk cows were infected with tuberculosis. It was in this way that swine became so extensively tuberculous. A man feeding milk to his hogs, if his dairy herd was free from tuberculosis, had no tuberculosis among his hogs, but when the milk began to be carried to the separators and creameries and the farmer took back not the milk from his own herd, but a mixture of milk from many herds, tuberculosis in hogs was almost the rule. This I believe is now prevented by law. But, of course, that is only for hogs which are of value commercially. For our children no such protection exists. Tuberculous milk from tuberculous herds is peddled around in nearly every city in this country, and the little children who are infected with bovine tuberculosis are to be met with on every hand.

Koch, in a series of experiments, thought he proved that bovine tuberculosis did not attack the human being. All he did, however, was to demonstrate that healthy cattle did not acquire human tuberculosis. We already knew that healthy human beings would not take tuberculosis. It required a breaking down, so to speak, of the constitution of the human being or of the cattle to permit the development of the disease.

I think it can be said at the present time that localized tuberculosis of the bones, joints, intestines, and glands is usually due to the bovine type of bacilli, and obtained from infected milk. Milk is infected not only with tubercle bacilli, but with septic bacteria as well, and these latter micro-organisms set up lesions in the gastro-intestinal canal, marked in younger life by gastro-intestinal irrita-

tion.   Through these lesions the tubercle bacillus gains entrance to
the circulation.   One of two things must be done: milk must be
pasteurized and no milk allowed to be sold that has not been
pasteurized, or else it must be certified from herds that have been
carefully tested for tuberculosis and in which the milk is gathered
with extreme cleanliness.   The pasteurization of milk is and has
been employed in many cities.   In Philadelphia, all milk will be
pasteurized.   Heidelburg, which was notorious for its tuberculous
children, has been almost freed from the white plague by the pas-
teurization of milk.   It simply means heating the milk up to 160°
under proper conditions, which not only kills the tubercle bacilli,
but the bacteria of sepsis as well.   It is probably to-day the most
practical way of handling the milk question.

CANCER

Much of the cachexia of cancer is due to associated sepsis, and
much of the pain comes from septic infection.   In the latter stages,
and especially where there are metastatic deposits, nerve pressure
may be the cause of very severe pain, as in "paraplegia dolorosa."
But the rule holds good that in the primary growth the action of
septic bacteria on the necrosed tumor and the pyogenic infection of
the surrounding tissue, already sadly crippled by the malignant
change, are the causes of the greatest distress and hasten the death
of the patient.   In internal situations, such as the liver, where the
growth is not exposed to infection, the tumor may often reach
large proportions and the patient die without severe suffering.
Gould found in the Middlesex Hospital, London, that careful
attention to cleanliness and antiseptic measures gave so much relief
that morphin was seldom required; even further, that patients
could not only be relieved of their pain, but that the symptoms were
so greatly ameliorated that they gained in strength and flesh
merely by scrupulous attention to cleanliness.

Bland-Sutton believes that the mortality following operations
for cancer is to a great extent influenced by the amount of sepsis
present, and especially by the character and virulence of the invad-
ing bacteria.   Cancer of the cervix uteri, by reason of the virulent

streptococci present in its sloughing recesses, gives a high mortality following radical operation; and without question much of the benefit which follows the application of heat and radioactive substances in cancer of the uterus is due not only to the destruction of the growth itself, but also to the destruction of the bacteria present. Bland-Sutton points out that the great mortality which has marked radical operations for cancer of the large bowel and rectum is due to septic complications. It was the high mortality of primary resection of such colonic growths, especially those beyond the splenic flexure, which led to the two-stage operation of Mikulicz, Bruns, and Paul. In this procedure the diseased portion of the large bowel is lifted from its bed with the fat and glands and brought outside the body, and left to remain in this position until it heals in. The involved sigmoid may then be cut away, and after the parts have been rendered reasonably sterile, the continuity of the intestinal tract can be restored by an operation which is largely extraperitoneal. In this way the mortality has been reduced one-half. In the rectum the same result is obtained indirectly by first doing a colostomy and subsequently carefully cleansing the lower fragment for some days before doing the radical operation, again reducing the mortality one-half. So true is this that an apparently inoperable growth in the rectum, fixed and adherent, may often be so benefited following colostomy and cleansing as to become operable.

There is a type of cancer which is often called inflammatory— a foul, indurated ulcer, covered with sloughing material, with an extensive inflammatory zone, brawny and red in character. If operation is attempted in this condition, the patients are seldom cured of the disease. The lymphatics in the vicinity become loaded with cancerous material from the cut surface, and metastasis quickly takes place. If such a condition, however, is treated by slow coagulation with the actual cautery, the parts will become clean and healthy, the bacteria and cancer both being destroyed. When the induration and inflammatory zone have completely disappeared, the entire area may be removed, with plastic repair of the defect. In this way patients can be cured who would otherwise be hopeless.

I examined a woman recently who had been to us twenty years ago with a cancer involving the cicatrix of a burn on the buttock received when she was a child. There was a sloughing, foul, indurated cancer and an inflammatory zone, altogether the size of a dinner-plate. Under an anesthetic this was thoroughly cauterized with the actual cautery, charring it until a perfectly dry eschar was obtained. This was treated with dry boric acid until it separated, which required several weeks. For fear some of the cancer might have been left, the entire area was then removed with the knife and skin-grafting done. Permanent cure followed.

About the mouth the same conditions often obtain—red, brawny tissue surrounding the cancer as a result of infection. Here the thorough use of the actual cautery, as advised by Ochsner, frequently prepares the field for successful operation.

Heretofore we have not given sufficient attention to the septic complications of cancer, especially in relation to preparing the field for operation. The extraordinary change which may be made in a growth by sterilization of the field must lead us to the conclusion that not only is sepsis a cause of serious symptoms to the patient, but that it is a most serious condition considered from the operative standpoint, and that the success or failure of an operation may depend as much upon the septic condition as upon the cancer itself.

We say that cancer is malignant in proportion to the ratio of cells to the stroma, the cells representing the cancer, the stroma the resistance of the patient. Many patients have comparatively little resistance to the cancerous cell, but react vigorously to a burn, throwing out an enormous amount of connective tissue, which may strangle the few cancer-cells that have not been destroyed by the cautery itself.

It has been shown that the cancer-cell, like all embryonic cells, is especially injuriously affected by heat, and that the difference between the normal cell and the embryonic cell of cancer in this respect is from 15° to 30°. Based on this, Percy, using a rheostat and an electric cautery, has introduced a method for the application of heat by a slow cooking process, keeping within this marginal difference. In this way the heat, in a manner, reaches out into the tissues and destroys the cancer-cell beyond its injurious effect on

the normal tissues. We are now applying the Percy method to infected cancers in all situations.

SUMMARY

1. The important rôle of associated septic organisms in the three most wide-spread plagues of mankind—syphilis, tuberculosis, and cancer—is not generally appreciated.

2. Much of our conception of the primary lesions of syphilis is based on appearances due not to the spirochæte alone, but to associated septic organisms. Because of the lack of hardness in the base, a hardness due to sepsis, not to syphilis, the diagnosis of chancre of non-venereal origin is apt to be missed in these days of cleanliness and antisepsis. The diagnosis should rest on microscopic evidence, the finding of the spirochæte in the chancre, and, later, by serologic evidence rather than on the gross appearance of the secondaries, the accentuation of which is due to sepsis and, therefore, in clean people may not be a prominent feature. The importance of a correct early diagnosis in the prevention of systemic infection cannot be overestimated. If this great opportunity is missed, early diagnosis will at least enable careful curative treatment.

3. Most patients afflicted with tuberculosis do not die from the disease, but from the associated sepsis. The surgeon must use great care in operations on pure tuberculous lesions to prevent secondary infections with other organisms, and not drain on account of the danger of subsequent infection, unless mixed infection is present.

4. Tuberculous peritonitis secondary to tuberculosis of the Fallopian tubes is often pure and seldom causes extensive adhesions. The proper treatment is the removal of the tuberculous tubes and closure without drainage.

5. Peritoneal tuberculosis having its origin in the intestine is liable to be a mixed infection from the start, and produces a distended abdomen filled with adhesions.

6. In tuberculosis of the kidney septic infection is responsible for many of the gravest symptoms, though in a large majority of tuberculous kidneys for which nephrectomy must be done there is

no active septic complication. When mixed infection exists, the ureter should be drawn up and stitched to the skin following nephrectomy. When it is absent, the ureter, if patulous, should be injected with 5 to 10 minims of carbolic acid, sutured, and dropped into the wound, which should not be drained.

7. The draining of pelvic tuberculous infection by an incision through the vagina may result in mixed infection and prolonged septicemia, with multiple fistulous openings into the bowel, often causing the death of the patient.

8. Much of the cachexia of cancer is due to associated sepsis, and much of the pain comes from septic infection. Cleanliness and antisepsis give great relief.

9. The high mortality following radical operations for cancer of the large bowel and rectum is mainly due to sepsis, and may be reduced one-half by two-stage operations. As much may be said in advanced cancer of the cervix when the preliminary cauterization with the actual cautery, especially the Percy method, followed by a complete hysterectomy, gives greater promise of cure with a smaller mortality.

10. Cancers of the surface of the body, covered with a sloughing material and surrounded by an extensive inflammatory zone, should be destroyed with the actual cautery, and when the induration has disappeared, the entire area may be removed, with plastic repair of the defect.

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SURGERY IN RELATION TO LIFE INSURANCE*

WILLIAM J. MAYO

Enlightened socialism is the key-note of modern civilization. Property rights have heretofore been considered sacred; human rights, of less consequence. On every hand we see a change of attitude in this regard, not alone in our country, but equally so in Europe. Even in the Orient the rights of the individual are now coming to be seriously regarded.

It has been customary, on just what basis I do not know, to estimate the value of the life of a young emigrant at $5000. Figuring thus, the gift in human life from Europe to America is staggering in its immensity. Immigration brings a vast multitude of people who have been cared for during their young and nonproductive years by the country from which they came, to give their productive years to the development of America. So cheap has this gift been held that it has been considered "good business" to run industrial enterprises regardless of human life, to maim, cripple, and destroy, and, finally, to throw on the human scrapheap as worn-out machinery the industrial immigrants rather than to preserve their bodies by hygienic measures and accident-preventing devices. And why not? This apparently inexhaustible army of recruits from Europe which had cost America not a penny to bring to maturity was ever ready to take the places of those who had fallen.

To-day this condition does not exist. Immigration no longer supplies the demand. Economic conditions in Europe now more nearly approach those in America. It is true that in the Orient

there is an almost inexhaustible supply of cheap labor. India and China stand ready to man our farms and factories. But we must not forget that the Roman Empire was undermined by the great quantity of cheap labor which was introduced from the Orient and which drove the Roman farmers to the cities. An influx of cheap labor into this country would have the same effect as has been so wisely foreseen by the people of California. The industrial peril of the Oriental races is real and not fancied.

Vigorous raw material no longer comes in abundance, while that from the south of Europe, which does come, has no such industrial value as that formerly obtained from the Germanic races. The demand for labor exceeds the supply, and we are faced with the necessity of conserving the individual worker. Not alone must we prevent accidents and furnish better care to the injured, but we must also improve the hygienic conditions under which the worker lives, that he may work with greater strength and for a longer time. In other words, it is now "good business" to care for the worker.

Originally insurance was intended for the protection of the family when imperiled by the death of the bread-winner. The insurance problem presents itself now from a new angle, that of equalization of the distribution of sick—both from sickness and injury—between the individual and the community. Out of this grows the workman's compensation, for which the employer must figure into his original cost of production the cost of injuries to his employees. There is no longer, therefore, the incentive to throw aside the partially worn-out employee, but rather it is best to utilize his remaining ability to produce. The experience of European countries teaches that we may expect these forms of compensation soon to be extended to the sick and to the old, as well as to the injured. New forms of taxation are now being devised, not for the protection of property, which was the basis of original taxation, but a tax on property for the protection and betterment of the individual. Of these, the income tax is the entering wedge.

If the American people are to do their own work, the working life of every citizen must be extended at both ends. At fourteen or sixteen years of age those who are not preparing for advanced

education should begin to labor at such a time and in such amounts as a humane and wise labor law shall prescribe. On the other hand, the middle-aged man must be protected, through hygienic and other measures, that his ability to labor may be carried to a later period in life. The work of Irving Fisher at present promises more for the middle-aged man than any other movement with which I am acquainted, and by it a new field of usefulness and one greatly to their advantage is opened for insurance companies, viz., the reëxamination of their own risks. The insured must be taught how to live longer and more efficiently, how to take in time those diseases to which they are subject, and which, if allowed to go unchecked, may lead to death; and how, by skilled help, their lives and usefulness may be prolonged. Insurance companies may thus postpone the payment of their indemnities. The gain to them is manifest and direct—the gain to the insured is equally manifest and direct. The part to be played by hygiene and general medicine in this great movement is predominant. When people are systematically examined by competent medical examiners for life insurance, physicians and surgeons will no longer have to wait until disease is so advanced that the patient recognizes it himself. It can and will be treated at an earlier period, with a correspondingly better chance of success.

In anticipation of the questions which confront insurance companies, a review of what surgery has accomplished in its relation to the prolongation of human life is important. The insurance company must know with as much accuracy as possible to what extent an average risk has been increased by a surgical operation, and whether a patient will be benefited sufficiently by an operation to warrant the insurance company in urging that it be performed. If death may be averted or life prolonged by an operation, it then becomes a matter of economy for the company to have the operation performed as early as possible, that the fullest economic results may be obtained.

It will be manifestly impossible for me at this time to more than touch on some of the prominent phases of the subject, and I shall confine my remarks to a brief series of impressions as to the results

of surgery in gastro-intestinal diseases in their relation to life insurance.

In estimating the results of a surgical operation from the standpoint of insurance, a number of factors must be taken into consideration. First, as regards the death-rate. I am assuming in the statistics given herewith that the results are such as would be obtained by an experienced and skilful surgeon. The personal equation, however, cannot be completely eliminated, and the results will vary to a considerable extent, depending on the class of cases accepted for operation. In estimating the curability of the disease for which the operation is performed I am again assuming that the surgeon is a thoroughly competent one, and that he is familiar with and experienced in the methods of procedure. The curability of the disease must be judged by a suitable operation, which varies in the individual case and not by the statistics or results obtained following a certain operation.

The results following gastro-enterostomy for duodenal ulcer are very good. But a small percentage of cases may not be cured by this procedure, and in these the excision of the ulcer, with a plastic operation on the outlet of the stomach, while giving a slightly higher primary mortality, will yield a higher percentage of permanent cures.

There must be considered also the effects of the operation itself. For example, in the dra'nage of an appendiceal abscess, not only will there be an increased liability to hernia, but also, as the natural result of the disease itself and of the drainage, there is the remote but still possible chance of future complications, the result of adhesions which may later produce obstruction of the bowels. The drainage lowers the immediate mortality, but of itself introduces slight yet sure possibilities of future complications.

When we come to study the question of the curability of cancer, a number of important facts must be considered. We know that one woman in nine and one man in thirteen past thirty-five years of age die from cancer. We ordinarily assume that the patient who lives five years following a radical operation for cancer is cured, yet we know that this assumption is sometimes wrong,

since an occasional case will recur after five, ten, or even after twenty-five years. Shall these be considered as recurrences or as new cancers? An operation for cancer permanently frees the patient of the disease in a certain percentage of cases, but it cannot rid him of his liability to cancer nor does it furnish him any immunity to the disease. Therefore, a patient who has lived five years following a resection of the stomach for cancer, and who at the end of that period is free from the disease, is probably no more and no less liable to cancer of the stomach than the average individual. Cancer of the stomach is the most common form of cancer in the human body, constituting probably not far from 30 per cent. of all cases of cancer.

It must not be forgotten that chronic irritation is a common, in fact the most common, precursor of cancer. Ulcer of the stomach, gall-stones, diverticula of the large intestine, and many other irritative conditions in the gastro-intestinal tract are thus a direct cancer menace to the patient. So true is this that the removal of foci of chronic irritation is the only known prophylaxis for cancer.

Whether or not a patient who once has been afflicted with cancer can safely be accepted for life insurance is a debatable question; but all in all, I believe that this should not be a bar in selected cases to insurance.

Stomach and Duodenum.—In discussing the surgical diseases in the digestive tract I have in mind recent additions to our diagnostic resources, especially the Roentgen ray, and also newer operative procedures, which have changed our point of view very materially. Ulcers of the stomach and duodenum are in concealed situations. Their diagnosis was formerly a question of clinical observation, and methods of clinical examination were and are notoriously inexact. That which we could not see we could speculate about. Some of these speculations were correct, but not until it was possible to inspect the stomach and duodenum directly during life did we begin to get an adequate conception of the pathologic condition present and to estimate the percentage of correct diagnoses we had formerly made by purely clinical examinations.

An estimation as to the curability of any gastro-intestinal dis-

ease based on data that were accumulated previous to five years ago is practically worthless. We formerly believed that simple ulcers occurred in the stomach in 95 per cent. of the cases, but we now know that 75 per cent. of them are in the duodenum. We supposed that the condition was much more common in women than in men; we now know that at least 75 per cent. of the cases occur in men. We believed that the lesion was nearly always multiple; we now know that the lesion is single in 95 per cent. of the cases. We believed that the taking of food gave rise to pain; we find, on the contrary, that food gives relief to pain. Instead of the existence of hemorrhage in the large majority of cases, it is a diagnostic symptom in not more than 20 per cent. The large majority of individuals suffering from sudden hemorrhage from the stomach who have not had symptoms of ulcer preceding the hemorrhage and in whom the ordinary symptoms of ulcer do not follow the hemorrhage have no ulcer. Ulcer is usually found in the pyloric end of the stomach or in the duodenum close to the pylorus. The healing of the ulcer produces scar tissue. If we could accomplish what we have so often talked of in the past, that is, heal the chronic ulcer, the condition of the patient might, by reason of obstruction, be worse than before. Indeed, this result is often found as a natural sequence after many years of suffering, and when seen in the terminal stage, these patients are often supposed to have cancer and are allowed to die under that impression, though the disease is but simple ulcer with obstruction, infection, and tumefaction, and withal curable.

Ulcer of the stomach is not quite so favorable for operation as is ulcer of the duodenum, because of the frequency with which cancer is engrafted upon it, rendering it imperative to excise the lesion, if possible. A slight increase in operative risk is, therefore, accepted in order to secure better ultimate results.

One thousand eight hundred and forty patients have been operated on in our clinic for ulcers of the stomach and duodenum and their complications (December 31, 1913). Graham recently reviewed the histories of 600 of these patients operated on within the last five years, but all more than one year ago. He found that

91 per cent. were cured, or so greatly relieved that they considered themselves cured, and that 4 per cent. were improved. A few patients had not been relieved because of technical defects in the operation itself, which had either been improperly chosen or improperly performed. It is quite within the limits of truth to say that 98 per cent. of patients with duodenal ulcer and 95 per cent. of patients with gastric ulcer may be cured by a well-chosen, properly executed operation.

The operative mortality for duodenal ulcer, including all causes, is about 1.5 per cent. That of gastric ulcers, which include the large callous ulcers in which resection is necessary, is from 3 to 4 per cent. Complications arising as the result of the operation are extremely rare.

The methods of diagnosing cancer of the stomach have been so improved in recent times, especially by the Roentgen ray, which makes early recognition possible, that we may expect a yet higher percentage of cures following operation. The reëxamination for life-insurance purposes by competent medical examiners will have a great influence in the detection of such growths while they are yet in the curable stage. Resection of the stomach for cancer gives about 25 per cent. of five-year cures, and the operative mortality is about 10 per cent.

Disease of the Biliary Apparatus.—Gall-stones may be considered foreign bodies, and, other things being equal, the earlier these foreign bodies are removed, the better for the patient. So true is this that any patient otherwise well, but having gall-stones, even though they are not giving rise to much trouble, would exercise good judgment in having them removed. In patients who are good risks for operation the removal of gall-stones has only a small mortality,—not over 0.5 per cent.,—and the patient becomes a good insurance risk at the end of a year. When the gall-bladder becomes so diseased that it can no longer functionate, it must be removed. About 80 per cent. of our cases come to us in this condition. The mortality from cholecystectomy is about one-third per cent. greater than that from cholecystostomy. While this is not very much in general, it is everything to the individual who

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loses his life. Not only does delay necessitate more serious operations, but the possibility of cancer developing in a gall-bladder which has been chronically irritated must not be forgotten.

In our clinic about 7000 patients with diseases of the biliary apparatus have been subjected to operation. More than 3 per cent. of these had already developed malignant disease. From a number of these patients the gall-bladder and a considerable portion of the liver and parts of the ducts were removed, but in not a single instance in which cancer was grossly manifest at the time of the operation was the patient cured.

In a number of patients from whom a thick-walled, functionless gall-bladder was removed cancer was found in an early stage. Many of these patients have remained well, showing that it is not the character and location of the disease, but the late stage in which it is discovered, that is so fatal. A patient with gall-stones has six times as many chances of dying from cancer of the gall-bladder and liver as he does of dying from an operation for the removal of the gall-stones in an early stage of the disease. Also in delaying there is the danger that the stones may be pushed into the common duct, with secondary involvement of the ducts of the liver and pancreas. The disease is then no longer local, confined to an unessential organ, but it invades organs essential to life, and the patient cannot be assured so certainly of permanent cure. While gall-stones rarely form primarily in the ducts of the liver, a small but definite percentage of people who have had stones forced from the gall-bladder into the common duct afterward develop stones in the ducts of the liver itself. The immediate mortality of operations on the common duct is considerably more than for stones in the gall-bladder. Taking cases as they come, usually with jaundice, infective cholangitis, and changes in the blood incident to the disease, the mortality is probably from 5 to 8 per cent. Again, the chances for post-operative complications, such as hernia, etc., are also present as a result of the drainage so necessary to the primary recovery of the patient. No patient can be considered cured permanently until at least two years without symptoms have elapsed after an operation on the common duct.

The Small Intestines.—Considering their great importance, extent, and nature, the small intestines are rarely diseased, probably by reason of resistance brought about by their long heredity. Immediately beyond the stomach, which has the highest percentage of cancers, is the small intestine, which relatively has the least. We have observed 22 cases of malignant disease of the small intestine, of which 8 were operable. The number is so small as to have little bearing on the question of its relation to insurance.

The appendix and its diseases may be considered a closed book. Whatever the value the appendix may have as a lymphoid organ in earlier life, it has comparatively little function in later life, and, so far as I know, no physiologic evils have followed its removal.

Following interval appendectomies there should be no danger of intestinal adhesions or obstructions, nor should hernia follow in the line of the incision with such frequency as to be a probable source of future disability. In cases with abscess and drainage there is a small but definite liability to intestinal obstruction from adhesions, bands, etc., and of hernia. Even in such cases, however, the probabilities are that the individual who has lost his appendix is in no greater danger from such complications than is the individual who has not had his appendix removed of having trouble with it of any equally severe grade.

Surgery of the large intestine introduces some new and complex questions. Influenced by Sir Arbuthnot Lane, of London, many believe that in the colon lies the cause of serious ills which bring on degenerative changes in vital organs, and which are responsible for the larger percentage of patients who present the symptom-complex which we term neurasthenia. Short-circuiting the ileum into the sigmoid and removal of the large intestine are being practised for the relief of these conditions. The first half of the large intestine may be called a herbivorous organ, as it is found most fully developed in herbivorous animals, while the carnivora show little difference between the large intestine and the small. It has been shown that we now consume four times as much flesh food per capita as we did one hundred years ago. Decomposition of vegetable matter results in fermentations which produce mostly

harmless combinations; decomposition of meats results in putrefaction with the development of poisonous bodies. It is possible that man, by an increased consumption of flesh foods, is introducing into the large intestine—a herbivorous organ—products of putrefaction, and from this source much of the so-called intestinal intoxication may have its origin. The subject is so new, however, that it would not be profitable at this time to discuss its effect upon insurance.

Tuberculosis of the large intestine of the hyperplastic variety is more common in the vicinity of the cecum and ascending colon. It gives all the clinical symptoms, and, when removed, many of the physical appearances of cancer, and is often due to the bovine type of tubercle bacilli. It is usually localized, that is, the individual has no other evidences of tuberculosis. So far as our experience goes, all the cases suitable for operation have remained well after excision.

Intestinal Diverticula.—Diverticula, which consist of little pouches of mucous membrane, which have been pushed through the muscularis, may become inflamed and thickened, and when involving a considerable segment of the large intestine, usually the sigmoid may greatly resemble cancer. In 6 of the 34 cases which we have operated on cancer had already developed in response to the irritation produced by little balls of hardened feces in the tips of the diverticula. Obstruction of the large intestine is a not infrequent result of diverticulitis. Many patients with this benign process have died from obstruction of the bowels as a result of this disease. Others were supposed to have been cured of cancer because they remained well following colostomy.

It is important, therefore, when a tumor of the large intestine is removed, that it be examined microscopically by a competent pathologist to determine its exact nature. Operation for cancer of the large intestine gives favorable results. In our experience 50 per cent. of such patients have lived for five years and were apparently well at the end of that time. These good results are undoubtedly due to the scanty lymphatics of the region involved,

so that the process remains a local one until a late stage of the disease.

In conclusion, I wish to call attention again to the fact that the only known prophylaxis for cancer is the removal of sources of chronic irritation. I also wish to point out that the insurance company may, by means of the reëxamination of the insured, prevent many deaths from cancer and greatly increase the length of life of the insured. Further, many of the conditions to which I have briefly called attention are even more important in relation to chronic infections and anemias, which have been shown to be so frequently the starting-point of cardiovascular disease, chronic nephritis, and many other disabling and often fatal diseases.

RECENT ADVANCES IN ORTHOPEDIC SUR-GERY*

MELVIN S. HENDERSON

Within the last five years literature on orthopedic work has been very conspicuous. One seldom sees a journal that does not contain an article pertaining to orthopedic surgery, which in itself is proof that the medical profession as a whole is taking a keen interest in this work.

While other specialties have had their day, only to be relegated to the field of the general surgeon, orthopedic surgery has maintained its place, and, particularly in America, is more strongly than ever intrenched as a specialty to which an increasing number of men are giving their entire time. The chief reason for this, perhaps, is the fact that orthopedic cases entail prolonged and careful post-operative treatment, and the general surgeon, whose energy is taken up with cases of a more acute type, and with a large clinic to maintain, finds he has not the necessary time to devote to this task. Two years ago a Section on Orthopedic Surgery was created by the American Medical Association. There must be good reasons why a specialty should attain this established position.

An exhaustive review of the literature on the subject of orthopedic surgery would involve too much detail for a paper of this character. The writer, therefore, will confine himself to those subjects that have been prominently under discussion.

TRANSPLANTATION OF BONE

As a branch of orthopedic surgery, the successful transplantation of bone has probably been the most important. While many

good results have been reported in the transplantation of bone from one individual, or even from one animal to another, the best results have been attained in the transplantation from one area to another in the same individual. That foreign bodies may heal permanently in the living tissues is an established fact. Gluck,[1] Bircher,[2] and König[3] have recorded the successful replacement of bone by ivory. C. H. Mayo[4] used ivory successfully as an intramedullary plug to induce repair in fractures of various kinds. Heteroplastic transplantation of bone from animals was an early practice, as evidenced by the fact that in 1682 Jobi Meekren used a piece of the skull of a dog to fill a defect in the cranium of a soldier. The operation was successful, but the Church, considering it improper that a man should retain dog's bone in his skull, forced the surgeon to remove it. From 1810 to the present time Merrem,[5] Flourens,[6] Wolf,[7] Ollier,[8] and others have reported heteroplastic transplants. Many have cited instances of the death of the transplanted bone, but these were heteroplastic and not autogenous transplants. All emphasized the importance of the periosteum and the marrow substance, claiming the formation of new Haversian canals and the deposition of new bone about these canals by the osteoblasts. The exact value and the function of the periosteum have been questions of no inconsiderable interest. The work of Ollier,[8] published in 1876, showing that periosteum was the chief factor in the regeneration of bone, was accepted for years. Macewen[9] has probably done more than any other man to disprove this broad statement. A review of a large number of reported experiments shows a lack of constancy in the results obtained. One observer was able to grow bone from periosteum in a majority of his experiments, another in a minority. McWilliams[10] concluded that a bone-graft was more apt to live in its new habitat if the periosteum was retained, which, after all, is the clinically important question, and not whether the periosteum is capable of regenerating bone. Practically no one depends upon the periosteum to fill in bony defects or to repair fractures.

The transplantation of bone has been tried and advocated for many and varied conditions. Its great field of usefulness is to

repair fractures and to replace defects in bone. Albee[11] and Murphy[12] have both been prominent in bringing forward this work, and have greatly aided in its technic. In the treatment of fractures, the transplantation of bone may be said to be confined to the cases of delayed union. The metal plates so strongly advocated by Lane[13] should be used in recent fractures. Before the transplantation of bone was introduced, the metal plates were used in cases of delayed union, and in many instances were not successful, but in the transplantation of bone we have a procedure which will bring about union in practically all cases. There are two ways of using bone-grafts: the intramedullary and the inlay method. In the former, the medullary cavity is reamed out and the graft inserted according to the method described by Murphy.[12] In the latter, a trough is made for the piece to be transplanted and the graft laid in the trough, thus obtaining an anatomic approximation of periosteum to periosteum, cortex to cortex, and intramedullary lining to intramedullary lining. This method, which has been described by Buchanan,[14] Albee,[15] and the writer,[16] brings under the control of the surgeon a heretofore most discouraging group of cases. The bone-graft may further be employed for tuberculosis of the spine, as a wedge in the scaphoid in club-feet,[17] and as a means of stiffening tuberculous knees.[18] Its use, as advocated by Albee,[11] to bring about fixation of the spine in tuberculosis, has been tried quite extensively and has been enthusiastically championed. Albee and others have shown by postmortem specimens that the bone-graft becomes attached firmly to the spinous processes, which would seem just grounds for expecting much good from this spinal operation.

Extensive resection of bone may be made for malignancy and the gap filled in with a bone transplant. The tibia can furnish large pieces of bone, and, if necessary, practically the entire fibula may be used.

Some surgeons advise the use of bone transplant in the spine, as recommended in tuberculosis, for the treatment of scoliosis, particularly in cases following infantile paralysis. The spine should be straightened by plaster-of-Paris jackets, etc., as much as

possible, the graft placed, and the patient maintained in the corrected position until the graft firmly unites.   Thus far this method has been only recommended.   No series of cases has been reported.

SCOLIOSIS

Largely through the work of Abbott[19] the treatment of scoliosis has received great impetus.   Abbott's results were so much better than those obtained by older methods of treating cases in the erect or extended position that men immediately began to visit his clinic. He has experimentally produced and corrected scoliosis in a normal individual.   He believes it to be a flexion deformity, often induced by the faulty position of the child at the desk.   By twisting and by flexion back through the same path he claims to accomplish more than in any other way and reports cures.   The whole question of scoliosis has thus been reopened and widely discussed.

Schanz[20] pointed out that the majority of the scolioses seen in the process of development were not of the severe or malignant type, and many improve or remain stationary.   He emphasized the seriousness of the malignant type from an economic standpoint, and doubted that the school-desk was a very prominent etiologic factor in the production of lateral curvature.   He stated that all real scolioses came from a disturbance of the static load on the spinal column.   Lovett[21] emphasized the divergence of opinion concerning scoliosis and its treatment, stating that the term was too loosely applied, and that the functional and organic or structural should be sharply differentiated.   He spoke favorably of the Abbott method, and believed that it had, on the whole, distinct anatomic advantages and offered the greatest ease of correction.

Forbes[22] has called attention to the so-called rotation treatment.   He flexes the spine and rotates the patient by means of the arms.   In basic principles the method seems to be very similar to Abbott's.

TRANSPLANTATION OF JOINTS

The transplantation of entire joints has been successfully performed in a few instances.   The difficulty of obtaining suitable

material for transplantation and the uncertainty of the result have deterred many surgeons from attempting it. Tuffier has twice transplanted the elbow-joint. In one instance the joint was obtained from a fresh cadaver and held in cold storage for five days. Eighteen months after the transplantation there was good functional result. His second case was successful, but was too recent at the time of report. Lexer[23] wrote of the present progress in transplantation of the knee-joint. He cited a case examined six years after transplantation in which the roentgenogram showed partial absorption and conditions similar to those found in arthritis deformans, but motion and function were satisfactory. The flexion of this joint was not normal; there occurred a pseudo-arthrosis. He stated that all ankylosed joints are not equally suitable for grafting of joints, particularly tuberculous arthritis, which is apt to cause suppuration.

TUBERCULOSIS

In the treatment of tuberculosis of the bones and joints some advance has been made. Radicalism in tuberculous joints is practically confined to adults. Stiles[24] has reported the results of excisions in children. His operations were performed on advanced cases, and many showed considerable resultant shortening, though less than would be expected. Probably in this type of case the operative results were as good as, if not better than, if conservative measures had been used. Brandes[25] reported 27 resections in children operated on for tuberculosis of the knee, of which 14 cases resulted in firm bony ankylosis enabling them to become wage-earners. Osgood[26] reported 28 cases of excision of the knee in adults; in 14 nothing was used to hold the bones together, and in 12 metal plates or wire was used. Convalescence in the latter group was so much easier, and union took place so quickly, that he advised the use of some material to provide fixation and thus hasten ankylosis.

The question of whether the primary focus in a tuberculous joint is in the bone itself or in the synovial membrane is still under dispute. It would seem that either may be the site. Ely[27] stated

that the synovia was often the site of the primary lesion.   Stiles[24] stated that, in the majority of cases of tuberculosis of the knee in children, the primary site was in the synovia.   Fraser,[28] from Stiles' Clinic, recently presented evidence that the primary lesion is frequently in the bone in the metaphyseal area.

Injecting tuberculous joints is a treatment not freely used. Murphy[12] advocates it in septic conditions.   Brackett[29] advises the injection of joints through an incision which permits exploration and removal of tissue for diagnosis with 5 per cent. iodoform in olive oil.   He maintains that the solution must be injected under tension so as to distend the joint and allow the emulsion to get into all its folds.   Fenwick[30] and Cashman[31] advocate the use of tuberculin.   It is, however, but comparatively little used.

The Roentgen ray for treating tuberculosis of the bones and joints still has its advocates.   Iselin[32] and Schede[33] believe that, under proper dosage, it gives beneficial results.   Schede[33] states that roughened skin and cold abscesses are contraindications to the use of the Roentgen ray.   There is always danger of irritating the skin and the occurrence of late ulcers.   This is emphasized by Iselin.[32]

Heliotherapy is a treatment which seems to be gaining rapidly in favor.   Rollier,[34] of Leysin, has for some time been treating cases of tuberculosis of the joints and bones chiefly by direct sunlight at an altitude of 4000 feet.   The use of plaster-of-Paris and apparatus is dispensed with, and the patients are kept recumbent, with traction, to prevent deformities.   Starting in with short exposure of about five minutes, the time is gradually increased to two or three hours, every part of the body with the exception of the head being exposed.   Austin[35] claims that the efficiency of the sun's rays is much greater at high altitudes.   Vulpius[36] thinks the altitude not so important as Rollier would have it.   The consensus of opinion, however, is that these cases are greatly benefited by this method of treatment, and no doubt it will be more freely used in the future orthopedic hospitals.

A method of treating tuberculosis of the spine has been advanced by Hibbs.[37]   It does not involve any transplantation of bone, but is rather an osteoplastic operation, and consists of form-

ing an ankylosis between the spinous processes and the diseased area. Also, the lamina are ankylosed, thus forming a strong posterior splint of bone. By specimens obtained at postmortem Hibbs has shown that ankylosis is obtained. This gives another means by which the ankylosis so essential in the treatment of tuberculosis of the spine may be secured. It has the advantage over the transplantation of bone in the same condition since only one incision is necessary, and is consequently preferred by some, although technically a little more difficult.

Beck's[38] bismuth paste is still being used for the treatment of tuberculous sinuses, and in a certain percentage of cases is of distinct benefit in closing many sinuses. The best results seem to be obtained by Beck.[38]

SYPHILIS

Syphilis of the joints, as recently pointed out by O'Reilly,[39] is more common than has been thought. The Wassermann test should be freely used, and the parents should be examined also when the test is negative in the patient. No definite connection between rachitis and syphilis has been demonstrated, although many observers incline to this view.

CHRONIC INFECTIOUS ARTHRITIS

The group of stubborn arthritides, called variously rheumatoid arthritis, osteoarthritis, chronic infectious arthritis, etc., are under better control than heretofore. Rosenow's work in bacteriology has aided us considerably in their treatment. A connection between tonsillitis and rheumatism has long been recognized clinically. Rosenow[40] has shown that the Streptococcus viridans and hæmolyticus may be isolated in some of these cases in the tonsil, in the joints themselves, or in the glands draining the joint. By removal of the tonsils a considerable number of cases of this group clear up. A vaccine made from the tonsillar crypt secretions, or the joint fluid or the glands about the joint, has given good results. A certain number of cases in this group may be cured by these measures. Lane[41] claims that intestinal stasis is responsible for many arthritic conditions, and reports favorable results following

removal of the colon or short-circuiting the cecum to the sigmoid. This radical procedure has not been generally adopted, but the observation of Lane's patients under treatment must impress one with the fact that they are greatly improved, radical though the treatment may seem.

Treating these arthritic cases with the glands of internal secretion has accomplished very little. A primary focus in the genitourinary tract may be the site of the chronic infection, and local treatment often helps the condition of the joint.

ARTHROPLASTY

For many years an ankylosed joint, usually the result of acute infection and sometimes of tuberculosis, has been the most that could be given the patient. Manipulation under anesthesia was usually a failure. The elbow-joint was the one exception, resections being done on the elbow, with excellent results. Of late Murphy[42] has steadily operated on cases of ankylosis of the knee, hip, elbow, etc., in many instances with astonishing success. Not all cases in other hands have been successful, but here and there a good result has spurred men on to increased efforts. Baer[43] has also been working on these cases, using chromicized pig's bladder to interpose between the raw surfaces, where Murphy uses flaps of tissue obtained from the operative field or elsewhere on the same individual, e. g., the fascia lata of the thigh. These operations for mobilizing joints have not been generally undertaken, and are still *sub judice* in the minds of most operators. Better, however, than performing arthroplasty is the prevention of ankylosis. Murphy mentions the injection of formalin in glycerin, and the maintenance of extension to prevent the deformities so often seen in these cases. Many of the joints, if stiff, in the proper position are so useful that patients do not deem it necessary to submit themselves to an operation.

FRACTURES

The treatment of fractures, while not relegated to the orthopedic surgeon, for many reasons still falls naturally into his hands.

His knowledge of the deformities which frequently follow a bad fracture, particularly those in or near a joint, causes him to treat all of them as "potential deformities" (Jones[44]). The treatment of recent fractures is generally divided into operative or non-operative. There is an abundance of literature on the subject, and the general trend is to treat conservatively those cases that may be reduced and held so as to insure a good functional result. The operative treatment is used in cases that cannot be held in any other way. The use of the bone-graft aids greatly the treatment of non-union. A report of the Committee on Fractures (British Medical Association[45]) is very valuable, and as concise as could be expected when the cases are gathered from many surgeons. The Committee reported that the non-operative treatment in children gave almost as good results as the operative treatment. After childhood, better results were obtained by the operative method, though the group of cases reported was small. Later operations for deformities following the non-operative treatment do not give nearly as satisfactory results as early operations for the same bad type of fractures. Sampson,[46] using Lane's careful technic in 47 cases of fractures in children, was able to procure 97 per cent. perfect functional results and 88 per cent. anatomically perfect functional results. Success has been reported in the intracapsular treatment of fracture of the neck of the femur by the abduction method of Whitman.[47] The longitudinal and lateral traction of Ruth and Maxwell has also been used effectively.[48]

INFANTILE PARALYSIS

Infantile paralysis still continues its ravages. A severe epidemic in lower California, with a mortality of 25 per cent., has been reported by Patterson.[49] The prophylactic measures used have not seemed very effective. Rosenau[50] reviewed the Massachusetts State Board of Health report, which points to the stable-fly as the principal carrier. Sawyer and Herms[51] transmitted the disease by this fly from monkey to monkey in seven cases. Neustaedter[52] reported the disease contracted by two guinea-pigs, although not by direct inoculation. The guinea-pigs were living in a cage directly

beneath a monkey which had poliomyelitis, with a nasal discharge and typical paralysis. As pointed out by the editors of the Fourth Report in Orthopedic Surgery,[53] this is particularly interesting, for all the previous infections of animals have been by direct inoculation, never by contact infection. Flexner and Noguchi[54] have succeeded in growing globoid bodies, with which they have produced typical paralysis in monkeys.

The transplantation of tendons in cases of infantile paralysis has been advocated for some time. Too much was expected of the procedure, and many were disappointed in the results because they did not take into consideration that a tendon in which the muscle is weakened is often transplanted, and that it is being placed in its new bed at a mechanical disadvantage. However, the transplanted tendons generally have sufficient strength to assist in establishing stability. Those in the leg and foot have generally been more satisfactory than those in the arm and hand, where the movements are more delicate and intricate. Wherever possible, the bony or periosteal implantation of the tendon, as recommended by Drobnik[55] and Lange,[56] is insisted upon by many. Vulpius,[57] on the other hand, believed that, for general use, the union of tendon to tendon is the best method. All writers of experience warn against tendon transplantation before orthodox orthopedic treatment has been carried out to prove that the muscles called paralyzed really are hopelessly useless. The wearing of apparatus to remove all tension on paralyzed muscles and thus allow return of function should be insisted upon. The social status of the patient in many cases determines as to whether or not an arthrodesis is preferable to tendon transplantation. Lewis and Davis[58] have reported cases of free transplantation of fascia to replace tendons, which suggests that they might be used to elongate tendons too short for transplantation. Gallie[59] has had good results in retaining paralyzed feet in position by cutting the paralyzed tendons and fastening the distal end to the tibia or fibula.

Volkmann,[60] in 1870, said: "No one has yet succeeded in restoring the continuity of the path from the nerve-center to the motor apparatus, nor is it likely that this ever will be accom-

plished." Vulpius[57] says that "the impossible is to-day within measurable distance of attainment, and nerve transplantation has passed beyond the stage of interesting experiment." Dr. Stoffel,[61] of the Heidelberg Clinic, has undertaken to work out the anatomic structure of certain of the nerves so that the surgeon may definitely know where the fibers to certain muscles are to be located. Vulpius,[57] in his work, takes up the individual nerves and describes them. The operation has not been generally adopted, probably due largely to the difficulties of accurately isolating the fibers and the extremely definite anatomic knowledge necessary. On the whole, the results have not been as satisfactory as those of tendon transplantation.

SPASTIC PARALYSIS

In the treatment of spastic paralysis Foerster's[62] operation of resection of the posterior nerve-roots has attracted wide attention. Technically, it is a somewhat difficult procedure, and requires definite anatomic acquaintance with the region. Foerster[62] gave the mortality as 8.5 per cent. He emphasized that the operation should not be used indiscriminately, that only severe cases, where all the muscles of the extremity were more or less involved, should be operated on, and that many of the mild cases, where one group of muscles was mainly at fault, should be treated conservatively by tenotomies, training, etc. Epilepsy contraindicates the procedure. Werndorff[63] advised that the deformities and contractures be eliminated as much as possible before the operation was undertaken. In many cases this will be sufficient. Jones[64] stated that this operation had a limited field, and reported excellent results from division of the adductors and the maintenance of abduction, to be followed by educational methods. Gaugele and Gumbel[65] were not enthusiastic over the operation.

SARCOMAS

In the management of sarcomas the present tendency is toward conservatism, for the results of amputations in the malignant sarcomas have been unsatisfactory, while the results of conservative

treatment have been practically as good. Bloodgood[66] was probably the first to take the definite stand that giant-cell sarcoma should be treated conservatively, for, though pathologically they might be considered malignant, as far as the life of the patient is concerned they are benign. He advised cureting and transplantation of bone to hasten healing. His views were supported by traced cases. He suggested the substitution of the term "giant-cell tumor" for "giant-cell sarcoma." Coley's[67] work has attracted much interest, and his results with the use of the toxin demand attention. By the use of the toxins of erysipelas and Bacillus prodigiosus he seems to have held the disease quiescent for years in a case of round-cell periosteal sarcoma. He did not, however, recommend the substitution of toxins for surgery. He called attention to the difficulty of making a diagnosis between myositis ossificans traumatica and sarcoma, particularly in the femur.[68] The danger of sarcoma developing in the myositis ossificans should always be considered.

Cysts occur in many of the long bones, more rarely in the skull or small bones. The literature on the subject is abundant. A recent article by Elmslie[69] gave a clinical, rather than a pathologic, classification of such cases. His report was very complete, but, as he stated, it was difficult to decide whether we are dealing with new-growths of bone or simply disordered growths. There is no proof that they are inflammatory in origin. The treatment is conservative, even though it may be necessary to curet more than once.

CONGENITAL DISLOCATION OF THE HIP

Much has been said on antetorsion of the upper end of the femur as a factor in congenital dislocation of the hip. Lorenz[70] interferes only in cases with marked antetorsion, doing an osteotomy just above the knee. Galeazzi[71] places more emphasis on this condition, reporting 30 successful cases. He rotates inwardly, flexes and abducts, putting pressure on the greater trochanter.

Ludloff[72] is an advocate of the open operation in resistant cases. Sherman[73] advocates the open operation in all cases. He reports

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29 hips reduced by incision with no subsequent osteotomy. Of these, 8 have gone into anterior transposition, 3 have stable reposition, but have developed coxa vara; 1 has become completely ankylosed, with no demonstrable infection; in 1, infection caused death; 4 were not traced; 12 have functionally normal joints, showing 41.3 per cent. of successful results. He has reduced 27 hips by incision with an osteotomy following. Of these, 2 have gone in anterior transpositions; in 2, the nail failed to hold the upper fragment and the parts returned to their original conditions; 3 are still under treatment; 19 have functionally normal joints. In this group he has 70.3 per cent. of cures. One of the chief reasons for Sherman's advocacy of the open operation is that the capsule so often shows a constriction too small to admit the finger, and much too small to allow the femoral head to pass through it into the acetabulum. Practically, it is not proved that this operation is necessary, as surgeons are obtaining about the same percentage of cures by manipulative reduction. If, however, this constriction in the capsule and the antetorsion are so important, undoubtedly the more resistant cases will yield more readily to the open reduction and osteotomy.

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A SHORT VISIT TO THE SURGICAL CLINICS OF RUSSIA, FINLAND, SWEDEN, NORWAY, DENMARK, AND BELGIUM*

WILLIAM J. MAYO

INTRODUCTION

The advantages of travel for medical study are very great. One may read with profit of the various clinics and of the men who direct them, but this is in no way to be compared with the actual observation of the hospitals and with meeting personally the controlling minds. In this way one may obtain an insight into the psychology of the groups of scientific men, and return from such an investigation stimulated to better work and inspired to higher ideals.

For some years I have made, each spring, as my holiday, a trip to some of the European clinics, and have, on a number of occasions, contributed to the pages of some medical journal, usually The Journal-Lancet, the results of my observations. On many of these journeys Dr. Christopher Graham has been my companion; and his personality and rare judgment have added greatly to the pleasure and success of the trips.

In planning such trips one can get along very nicely with about two months' absence, and, with a well-planned itinerary, can visit the more important clinics of several countries. Even so short a time as one month in Europe is well worth while, since the distances, as a rule, are not great, and therefore very little time need be lost in travel, except for the ocean trip, which furnishes a usually much-needed rest. One leaves home tired out, but in the week of ocean

travel he has an opportunity to become well rested. In the return trip, again, one gets needed rest and recuperation just before returning to work.

To secure the best results, the trip should be planned a number of months in advance. The heads of the clinics which are to be visited should be written to at such time that the letters may reach their destinations early after the beginning of the school year. In this way one may ascertain whether or not the clinics will be running at the date of the proposed visit. Otherwise one may lose considerable time, as, for instance, by arriving at about the Easter holiday, at which time nearly all the Continental clinics have one or two weeks' vacation. It is well to verify the information received about two months before the journey by a second letter, and then, in reply to the almost certain note of cordial welcome, by a third communication about two weeks before departure, giving the exact date of the visit, and, if possible, even the hours of arrival and departure. One may thus be able to see those things which the clinic prides itself upon arranged in such manner as to be covered within the limits of the visit.

In order to get the most out of the trip, one should have a working knowledge of German, even though it be meager. English will carry one; but with the two languages one will have no difficulty in securing to the full the advantages afforded, except in the Latin countries. Fortunately, there the educated men generally speak English.

March and April are splendid months for visiting Italy. For France, Germany, and Switzerland the latter part of April, all of May, and the first part of June are much more pleasant for travel than in the summer, when it is hot and dusty, and these countries often uncomfortably thronged with tourists. The last days of May and the first days of June are very beautiful through the North Countries, and, as a rule, it is not too cold for comfort if one is supplied with proper wraps. At this time also the sight-seeing places, in addition to the clinics, may be visited. Study travel has the advantage that at least one-half of each day may be spent in seeing the country, the art museums, the universities, and other

places of interest, a knowledge of which contributes so much to those sources of contentment within ourselves which make us independent of our environment in later life.

RUSSIA

The approach to Russia is best begun from Berlin. There are two routes: one, the southern, by way of Breslau, Warsaw, Moscow, and thence to St. Petersburg; the other, the northern, directly to St. Petersburg, and thence a separate trip, if desired, to Moscow and back. We chose the southern entrance, as it gave us a wider view of the country.

Leaving Berlin about midnight, the next morning the traveler is at the border of Russian Poland, where he exhibits his passports and his baggage is examined. Passports must be obtained personally in New York, Chicago, or some place where there is a Russian consul. These passports must be carried continuously when in Russia. They must be presented at each hotel visited, where they are viséed, and returned as one departs. The examination of baggage and showing of passports on entering Russia are not more burdensome than the formalities of entrance into most other countries, and certainly compare favorably with the process of passing the customs into America.

POLAND

Poland is a splendid country, which lies on the German border, projecting as a great peninsula into the German Empire. It was divided up after the Napoleonic wars between Russia, Prussia, and Austria, Russia getting the lion's share. Within a few hours' ride from Poland's border is the great German city of Breslau. One always changes cars on passing to a Russian railroad, as its gage is some few inches wider than the standard gage of Europe and America. The cars are comfortable, the trains are on time, and, as a rule, the food in the dining-cars compares favorably with that in other countries.

The trip across Russian Poland shows a great, fertile plain with patches of conifers of sufficient size to be called forests. Roman

Catholic churches are in evidence, and the people are all at work, especially the women. Children under five years care for the geese; and old people, beyond the time of active labor, care for the cattle. There is no waste land.

On arriving at Warsaw, which is a great city of about 800,000 people, early in the afternoon, the train stops for nearly an hour, and one can get quite a view of parts of the city in this short time.

Toward evening one enters Russia proper. The physical appearance of the country remains about the same; but the Roman Catholic Church, which has been in evidence nearly everywhere, and the language, which has been Polish, suddenly disappear, to be superseded by the Greek Catholic Church and the Russian language. One hundred years has apparently failed to Russianize Poland or to affect its language, religion, or customs.

Russia is essentially a great plateau, from 500 to 1500 feet above sea-level. So slight an elevation in so great a tract of country gives poor drainage, and much low, sour ground is to be seen. The people live in communities and appear sad; and even the children do not play as in other countries, but in passing at the station one sees them solemn and serious—small replicas of their parents. Every one wears boots.

The conifers gradually change to birch as one nears Moscow, which is entered about 4 o'clock of the second day, the whole journey from Berlin being made in about forty hours.

As I read my rambling notes I fear I am not doing justice to the agricultural conditions of Russia. It should be explained that the Steppes, or Black Earth country, lies in the southern half, and it is here that the great agricultural regions of the country are to be found.

The route followed by train is most interesting from a historic standpoint, as it is nearly the route of Napoleon's invasion. One passes through Smolensk and Borodino, where the Cossack General Kutusoff met Napoleon in his invasion, and where bloody battles took place. Of especial interest was Borisoff, where Napoleon's army was broken up after the fatal campaign of 1812 by the Cossack general who struck him in his retreat on the stream near by,

which was then in flood and in which the dead bodies of horses and men with the artillery finally formed the bridge that let the remnant across to flee in a disorganized rout.

Moscow is one of the most interesting cities I have ever visited. It is real Russia, and has conditions which are unparalleled. It has a population of about 1,800,000. Its general interest is greater than its medical. The Kremlin, Red Square, St. Basil's Cathedral, and other remains of early Tartar control give it a charm which is quite its own. Here are to be found the Vereshchagin pictures, which rank with the great works of art in the world, and depict the horrors of war as they were scarcely conceived even by Dante. Vereshchagin's tragic death by drowning in the Russo-Japanese war, while in the prime of life, is deeply regretted by every lover of art. In Moscow also is the great orphan asylum built by the Empress Catharine, with accommodations for 40,000 children. War, pestilence, and famine have rendered the work of this great institution of tragic significance at various periods of Russian history. It is not conducted, as in many cities, for illegitimate offspring, but as a home and refuge in which parents may leave their children, and, when able, remove them into their own care again. Fortunately, the number of occupants at this time is small, as the conditions which cause crowding do not exist at present.

There are nine Russian universities, six of which contain medical schools, one for women. The entrance is essentially by competitive examinations from the gymnasia, which correspond to the German gymnasia and to our high-schools. The medical school in the University of Moscow has about 300 students.

I am indebted to Professor Dr. Martynov for an interesting visit to the surgical clinic. The wards were clean, the food was good, and I was much impressed with the linoleum in flowered patterns, which everywhere covered the floors and which added a little life and color, such as we seldom see in the material on our hospital floors, where it is usually of one color or in geometric patterns. The operating-rooms were modern, and in the clinical laboratories were eight workers. There was no training-school for nurses.

After spending two and one-half days in Moscow, we took the night train for St. Petersburg, about a twelve-hour journey. The country is flat, and there are many conifers, giving a gloomy aspect to a country with a sour soil. St. Petersburg is a modern European city, and has a population of somewhat over 2,000,000 people. It is situated on the River Neva, at the apex of the Finnish Gulf, and is only 15 feet above the sea. History records that Peter the Great, who built this city, lost 100,000 men the first year in his feverish haste to lay its foundations.

There are in Russia over 100,000,000 of people. Six millions, called White Russians on account of their peculiar dress, live on the western border adjoining Poland; 20,000,000 of the Little Russians, who are small and dark, live in the southwestern part, adjoining the Balkans; and 80,000,000 of the Great Russians, a large, strong people, very religious and sober in character. When speaking of "Russians," it is to the Great Russians that I refer.

The Russian alphabet contains 36 letters, derived from the Latin, with Greek additions, which gives a far-eastern cast to the writing and printing.

In addition to the 100,000,000 of people who speak Russian and belong to the Greek Church, there are about 50,000,000 of lesser groups and tribes, who speak about 150 languages and dialects. While Moscow is typical of the Russians, St. Petersburg, the capital city, shows many types and characteristics derived from outlying countries and tribes.

There are many points of non-medical interest in St. Petersburg. The Hermitage is one of the greatest picture-galleries in the world, and contains more fine paintings by Dutch and Flemish artists than can be found in Holland or Belgium. A trip to the Alexander III Museum, with its pictures by the great marine artist, Aivazovski, who is second only to Vereshchagin, and to the Imperial Winter Palace gives ample occupation for the time not spent in the clinics.

St. Petersburg represents intelligent, modern Russia. The University is the largest and best in Russia; and its hospitals are excellent, but many of them are open only six months in the year on

account of lack of funds.   I was told that it was considered wiser
to run them well for six months than to run them badly for a year.
Just what the people do when they are ill the balance of the time
I do not know.   Some of the largest institutions are so-called mili-
tary hospitals, that is, they are for the soldiers and for the soldiers'
families.   In nearly all the hospitals one finds a bust of the master
surgeon, Pirogoff, whose great work in the last generation gives
Russian surgery a distinctive character.

St. Petersburg has a splendid hospital devoted entirely to
obstetrics and diseases of women.   The building is ten years old,
and is so well planned for the purpose that it has been taken as
a model for similar institutions all over the world.   It takes care of
5000 obstetric cases a year.   The work is in charge of the distin-
guished obstetrician and gynecologist, Professor Ott, well known
through his splendid contributions to pelvic and abdominal sur-
gery.   He has a strong personality, is original in his conceptions,
daring in execution, and may be called the master of the vaginal
route for pelvic operations.   He especially champions vaginal
hysterectomy for cancer of the uterus as against total abdominal
hysterectomy of the Wertheim type.   He points out the exceed-
ingly low mortality of the vaginal operations (less than 3 per cent.
against 19 per cent. for the abdominal), the absence of serious
accidents, such as fistulas in one or both ureters, bladder, or rectum,
or both combined, which occur in the total abdominal operations in
from 4 per cent. to 7 per cent. of the cases, and that the total per-
centage of cures with the vaginal method is within 6 per cent. as
great as with the abdominal.   When the mortality is taken into
consideration, the difference in permanent cures, he believes, favors
the vaginal rather than the abdominal route.   I witnessed him carry-
ing out his method of vaginal hysterectomy for cancer of the cervix—
wide incisions for exposure, removal of the uterus, followed by re-
moval of the ovaries and tubes, ligation of the vessels and lateral
ligaments with heavy silk, the ends of which are left long for later
removal, and always packing the pelvic cavity with iodoform
gauze.   No sutures are used.   I was much impressed with his care-
ful hemostasis.   He uses retractors of the spoon-bill type, each

with an electric light carried down to the end, which illuminates
the entire field of operation, the patient being in the perineal posi-
tion with the hips elevated.   With very long retractors of the same
type he can make a fairly good exploration of the abdominal cavity;
and in one case he was able to show me the liver, stomach, and
gall-bladder through the vagina.   With similar electric-tipped re-
tractors he demonstrated the rectum, lower sigmoid, and bladder.
So far as I know, Ott's mortality by operation through the vagina
is the smallest of any one in the world.   For all cases, including
cancer, in a consecutive series of 500, the mortality was 0.37 per
cent.   Professor Ott speaks English.

Professor Fedoroff, of the Imperial Military Hospital, is an
excellent surgeon, and has a justly earned reputation for surgery of
the kidney.   He has a remarkable collection of specimens illustrat-
ing this type of surgery, and I had the pleasure of seeing him operate
on several cases.   One was a nephrectomy for pyonephrosis with
stone in which he did the subcapsular operation.   Very interesting
and instructive in detail was the handling of the vascular pedicle.
After drawing the kidney well up into the incision, the capsule
slipping back, he split the capsule circularly about the pelvis so
that the entire pedicle of the kidney slipped through the opening,
thus permitting careful ligation of the vessels.   I was interested
to know that he prefers pyelotomy to nephrolithotomy for stone in
the pelvis of the kidney.   Professor Fedoroff speaks German.

Professor Roman Werder, Chief Surgeon of the Orthopedic
Institute, is well known in America, which country he has visited
on two occasions.   He was Surgeon-General of the Russian army
during the Russo-Japanese War.   The hospital, which he controls,
is very complete; and in the extent and variety of its manufacture
of mechanical appliances I have seen none better.   The workshop
is so great in extent that it resembles a machine manufactory.
Professor Werder is very much pleased with the Albee operation
for tuberculosis of the spine, and he showed me a number of such
cases.   He is very conservative in his view of the operative treat-
ment of tuberculosis of joints.   He speaks English.

Professor Turner is the Surgeon-in-Chief of the Orthopedic

Department of the Military Hospital.   He is English, or at least was born of English parents in Russia, and English is his native tongue.   He is carrying on a very interesting piece of research work in connection with fractures of the neck of the femur.

Professor Herman Zeidler is chief surgeon of the Women's Medical School.   He controls a fine hospital of about 100 beds, and has much interesting clinical material.   He speaks German.

FINLAND

After the Napoleonic wars, Finland, which had been under Swedish control, and had advanced under Swedish influence to a very high state of civilization, was given to Russia, and became a Grand Duchy, but was granted its own constitution and control of its internal affairs in the same manner that the British colonies, such as Australia, control their affairs.   For nearly one hundred years this worked well, the Finns continuing under Swedish influence, developing a high state of civilization, with only 1.5 per cent. illiteracy.   About ten years ago an attempt was started to Russianize Finland.   Their constitution, which had been held inviolate, was abrogated in part without their consent.   It is pitiful to see the national despair of this cultured people of nearly 3,500,000 under the shadow of Russia.   Whether Finland's fears will be justified, only future events can tell.   The Russian people, so far as I could learn, are naturally kind, dignified, and faithful; and the educated Russian is the equal of any man.   The rapid building of railways, highways, and waterways in Russia will soon make a great difference in general education, as ease of communication is the greatest factor in civilization.   Perhaps Finland may not be so badly off in the end.

The Finnish people are derived from the Mongols, but have been so thoroughly intermingled with other peoples, especially with the Scandinavians, that they have little of the Mongol's physical appearance.   The schools of Finland teach six languages: Finnish, Swedish, Russian, German, English, and Latin.

Finland is called the "country of lakes."   It has but one university, which has between 2000 and 3000 students, and is situated

at Helsingfors, a beautiful city of 150,000 inhabitants. Ali B. Krogius is chief of the surgical division of the University Hospital and Professor of Surgery at the University. He is a master surgeon, and the equal of any surgeon in any country. He speaks German.

I saw much to interest me in Helsingfors, of which time and space preclude more than a passing word. Professor Krogius exhibited some cases of both simple and multiple osteomyelitis fibrosis, in all of which a diagnosis of sarcoma appeared probable. He called attention to the necessity of greater care in differentiation to prevent unnecessary mutilating operations. Actinomycosis is common in Finland, and I saw a number of cases of that disease.

One of Professor Krogius' clinics which I attended contained three interesting cases for operation. The first of these was a case of spastic paraplegia in a boy of seven years. Two weeks previous Professor Krogius had removed the spines and lateral processes of the lumbar vertebræ. When he opened the wound, I was surprised to see how much fluid was contained within the membranes of the cord. When they were incised, about three ounces ran out, evidently the result of traumatism of the first operation. He removed the sacral posterior, sensory roots, and the spasticity immediately disappeared. Ether was used with the head lowered. The second case was a boy, aged eighteen, on whom he did a resection of the left third, fourth, fifth, and sixth ribs from the sternum to the posterior axillary line for pericardial adhesions. The boy had had pericarditis some months before, with effusion, and this disease had left greatly impaired action of the heart. Professor Krogius had operated upon several cases in this manner with great relief. Local anesthesia was used, with a moderate amount of ether. The third case was one of exstrophy of the bladder in a boy aged one and one-half years. This operation was made under ether with the head low. A ureteral catheter was inserted into each ureter and sutured in position. The bladder, except a fragment containing the ureteral orifices, was dissected away, the abdomen opened, a loop of sigmoid brought out, and an entero-anastomosis made between the afferent and efferent limbs.

The piece of bladder containing the ends of the ureter was then sutured to the apex of the excluded loop of the sigmoid.

Professor Sandelin is Surgeon-in-Chief of the Helsingfors State Hospital, which is a very bright and cheerful institution. He is a clever surgeon and speaks English. I was greatly interested in his method of preparing silk suture material. To those of us in America who use very little of the buried sutures except catgut, the freedom with which silk is buried abroad is interesting. I saw Professor Sandelin closing hernias with buried No. 2 silk in quantities that I would not have thought advisable. He says that silk should first be put into ether for twelve hours to remove the fat, then into alcohol for four hours, after which it should be boiled for ten minutes in 1:1000 bichlorid solution. It should be boiled for five minutes each time before using in 1:1000 bichlorid. This soon destroys its strength, and only small quantities are prepared at a time. If the fat is not entirely removed from the silk, it protects some part of it from the action of the moist heat, and the part so protected will only be subjected to dry heat at 212°, which will not be sufficient to sterilize it.

Professor von Bonsdorff, Chief Surgeon to the Deaconess Hospital, whom I had the great pleasure of meeting in America, was not at home. I visited his clinic, which is an excellent one, with 100 beds for adults and 40 for children.

I regret exceedingly that I did not see any operations by Dr. Bjorkenheim, of the Gynecological Clinic, whom I had previously met in America, since I was told that his clinic is a most interesting one. With characteristic modesty, he had arranged that I should see all the others, and had left no time for his own work.

SWEDEN

The trip from Finland to Sweden was one of the most magnificent sea voyages I ever made. Leaving Helsingfors about 10.30 A. M., we continued down the Gulf of Finland, threading our way in and out among thousands of islands along the Finnish coast. These islands extend well out into the Baltic, so that when we crossed the Baltic we were out of sight of land only one and one-

half hours.   It was quite light until after eleven o'clock at night, and we were out early the next morning as we came through the thousands of islands in the narrow projection of the Baltic Sea, at the apex of which Stockholm is situated.

Stockholm is one of the most beautiful cities in the world.   Its situation at the head of this arm of the sea, its islands, and its beautiful buildings, give it an individuality which is quite its own.   I had looked forward to the trip through Norway, Sweden, and Denmark with very great interest.   In all my previous trips to Europe I have at various times made plans to go into the Scandinavian countries, but something always prevented.   Because of the great number of Scandinavian people living in Minnesota with whom I had had most pleasant professional relations, it seemed like visiting a home country, and I was not disappointed.

At the risk of appearing pedantic, I want to say a few words about Sweden and her people.   The countries that I had just visited, Russia and Finland, have been very forcefully affected by the Swedes, who at one time controlled a large part of western Russia, even as far south as Moscow, and had it not been for the unfortunate death of Gustavus Adolphus in battle, might still be in control.   This disaster, followed later by the misfortune due to the rash courage of Charles XII, left Sweden with 5,500,000 people confined to the Swedish peninsula, after exerting an extraordinary influence on the civilization of the countries which she at one time controlled.   I speak of this because now in Sweden the shadow of Russia has its terrifying aspect.   They have 400,000 trained militia, and they are building battleships appropriate to their waters, and all with the idea that their national existence is threatened by Russia.   They are a peace-loving people, cultured, and the equal in civilization of any people in the world.   A leader in great educational movements, such as manual and industrial training in the schools, in science and the arts, Sweden is a country of which any man should be proud.

One of the greatest charities I have ever seen is in Sweden. Epidemic poliomyelitis is sometimes called the Scandinavian disease.   In 1912. 4000 people were permanently crippled from this

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cause.   Sweden operates institutions for teaching cripples of all
sorts how to make a living.   Under scientific methods,—transplan-
tation of tendons, etc.,—and by the application of appropriate
apparatus, the cripples are first benefited physically to the greatest
possible extent.   Then a careful study is made of each individual,
and he is taught a trade with which his disability will not interfere,
and furnished with special tools for carrying it on.   It is extraordi-
nary how proficient many of those cripples become; and, instead of
being a permanent charge upon the State, they are converted into
self-supporting citizens.

Sweden has four universities, two of which are complete.
Upsala and Lund possess all of the faculties, and Stockholm and
Gothenburg have incomplete universities, possessing some of the
faculties; but neither has a medical school.   The medical school in
Stockholm is not directly connected with the university of that
city, but is under the direction of the State, controlling a State
hospital, which acts as its clinical laboratory.   The university at
Gothenburg has no medical department.

Professor John Berg is the chief of the Surgical Department of
the Stockholm School, a man beloved and honored by all who know
him.   Nearly all the important surgeons that I met expressed their
veneration for this man, and spoke with great pride of the fact that
they had at one time been among his assistants.   Imbued with
great energy and a desire to inspire younger men and create sur-
geons, Professor Berg has been wonderfully successful.   He speaks
English.

In Professor Berg's clinic I saw an electric-lighting device for
examining the pleural and abdominal cavities which was very good.
A trocar was introduced with a cannula, the fluid withdrawn, and
an electric light introduced through the cannula, much like a cysto-
scope.   The view was remarkable.   With ascites in the abdominal
cavity in connection with carcinoma of the liver the same result
was achieved after removal of the fluid.   The liver, with its can-
cerous nodules, could be quite plainly seen.

Professor Åkerman, who is associated in the hospital with Pro-

fessor Berg, speaks excellent English, and has a fine reputation as a surgeon.

There is a large number of surgeons of high character in Stockholm. Of the younger men, Key seems to be most universally admired. He has 120 beds in the Municipal Hospital, and is a surgeon of great industry and marked originality. He showed me a number of cases in which he had removed a tuberculous kidney from one side. The ureter connected with the sound kidney on the opposite side had been opened in the loin, and an ingenious apparatus made to collect the urine. Several of these cases had been done a number of years; the patients were quite dry, very comfortable, and able to work. The intention had been to relieve from urinary irritation the ulcerated and permanently damaged bladder, the frequent and painful micturition being in this way obviated, as the bladder was thrown out of commission.

I saw also in Key's clinic a number of interesting cases that had been operated upon for ulcer of the stomach and duodenum and for deformed fractures. Key speaks English moderately well.

Professor Toll, Chief Surgeon of the Deaconess Hospital, spent seven years in America. He has a beautiful hospital, with perhaps the finest view of the harbor and city in Stockholm. I especially appreciated my welcome here, for when I came up to the door a large American flag was suspended in the breeze. Toll speaks English.

Waldenström, one of the young surgeons at Stockholm, is connected with the Institute for Cripples. I saw there some most remarkable cures of deformity of the spine from Pott's disease. A plaster case is made, the anterior half is completely removed, the child lies in the posterior half, and every week or two little strips of felt are arranged to bring pressure on the kyphos. The child can be removed from this case at any time, but must lie on the face, and is never allowed on the back or side except in a plaster frame. In one or two years, up to the age of ten, these patients are completely straightened. He then does an Albee operation, introducing a piece of bone from the tibia into the spine, and securing permanent results.

I had a very interesting visit with Dr. E. Gunnar Nyström, an exceedingly capable surgeon, assistant to Professor Berg, who visited America some years ago.   I also met Dr. H. S. Hübinette, who is not only one of the most successful surgeons in Sweden, but is a great tenor singer as well.   He is called the Swedish Caruso.   He has had extraordinary offers to take up singing in grand opera as a profession, but has always refused, for he is interested only in surgery.

The best x-ray work that I saw on this trip was that of Professor Forrsell, of Stockholm, in connection with the medical school. Much of the apparatus is of his own invention, and all over the Scandinavian countries his methods have been largely adopted. He uses a tinted glass for plates, as it furnishes a clearer background for differentiation.   He also has charge of the therapeutic work with radium and the x-ray.   He says that 30 per cent. of all sarcomatous growths can be made to disappear with radium, but that every case has relapsed within four years; and that in carcinoma he has been able to cure only superficial growths, but, when so cured, they have remained well.

Upsala, about 40 miles from Stockholm, is the great university town of Sweden.   There are more than 2000 university students. The University Hospital is well equipped, and has a splendid organization.   It was made famous during the lifetime of its great surgeon, Lennander, who died about five years ago as the result of long-standing heart disease.   Lennander's work is best known to Americans through his study of visceral and parietal sensitiveness of the peritoneum, and also in connection with the pericolic membranes.   For many years he was able to work but a short time each day, lying in bed between times, yet having but a single idea, to continue in his beloved profession and advance its interests to the last.

Professor Ekehorn has taken Lennander's place.   He has a splendid reputation, but on account of a death in his family I unfortunately had to postpone my visit to his clinic until some future time.

Lund is a city of 35,000 inhabitants, and has a complete uni-

versity.   Professor Borelius, who visited America some three or
four years ago, has charge of the surgical department.   Looked at
from every standpoint, Borelius is one of the best surgeons with
whom I am acquainted.   My time in his clinic was most profitably
employed in taking notes for future reference.   I saw here a most
interesting case of plastic bone flap for hernia cerebri, the use of the
transverse incision for work on the gall-bladder and ducts, which
gave splendid exposure, and the use of needles passed through in
such a manner as to fasten movable bodies in the knee-joint so that
they could be removed with ease under local anesthesia. He speaks
English.

Professor Essen-Möller has charge of the gynecologic clinic, and
does most interesting work.   He told me that between 5 and 6
per cent. of his cases of hysterectomy for myomatous disease showed
associated malignancy.   He was not enthusiastic about radium for
the cure of cancer of the uterus, but said that he got palliation with
it.   He speaks English.

Malmö has about 100,000 inhabitants, and has one of the most
modern hospitals in Europe.   The surgical department is under
Dr. Fritz Bauer.   To those interested in building a new hospital,
the equipment, arrangement, and organization of Bauer's clinic is
an example of efficiency.   I saw him do a number of very brilliant
operations.   He had recently successfully removed a large embolus
from the abdominal aorta which blocked both common iliacs.   He
speaks English.

Bauer's assistant, Dr. Otto Löfberg, has developed a method,
much like that of Royal Whitman, for the treatment of intracap-
sular fractures of the hip-joint.   It consists of extension and rota-
tion inward of the affected limb under anesthesia.   The limb is
then placed in a plaster-of-Paris case, which is worn for twelve or
fourteen weeks.   The patients are allowed to ambulate when they
are able, usually in from ten to fourteen days.   He had treated 100
cases in this way at the time I visited Malmö, with 98 successes.
I had the pleasure of seeing a great many of the skiagraphs that had
been taken, and the results were remarkably good.   Only one
patient had died—a female aged eighty-four years.

In all the hospitals I visited in Sweden the anesthetic was given by nurses in about the same manner as in America, that is, by the drop-method.   There are excellent training-schools for nurses, with two-year terms, which will soon be extended to three years.

NORWAY

Norway has somewhat over 2,250,000 people, and is under a Danish Prince, having separated from Sweden about ten years ago. The Norwegian language is practically the Danish language, with the addition of some original Norsk, and has been in its present state for about five hundred years.   Since separating from Sweden, many Norwegians have endeavored to bring the original Norsk language into existence.   It is permitted to teach either in the schools, but I was told that the idea of replacing it by the ancient Norsk was not very favorably received.   There is but one university in Norway, at Christiania, to which both men and women are admitted.

The university has two surgeons of equal rank: Professor Joh. Nicolaysen and Professor Edv. Bull, each having a clinic and hospital beds.   These surgeons have an international reputation. Professor Nicolaysen has recently visited America, and is personally known to a large number of Americans.   He speaks English, as does also Professor Bull.

I saw a number of exceedingly interesting things in the University clinic.   Actinomycosis, which is quite common, is treated by radium, some cases being cured by a single application.   Angioma and lymphoma and apparently sarcoma and an occasional case of carcinoma have been cured by radium.   Professor Nicolaysen showed me some interesting cases of tuberculosis of the intestine, demonstrating that the points of bacillary entrance were microscopic; that the disease is always more extensive in the intestine than it would appear from macroscopic examination; and that it is, therefore, necessary to remove a considerable length of apparently sound intestine on each side of the visible disease.

Professor Bull, in doing a nephrectomy, sutured the stump of the ureter to the skin, a method which I had seen practised by

Zuckerkandl, of Vienna, and others. He said that it always healed in a comparatively short time.

I was very much impressed with the Christiania Medical School and the medical students. At one of the demonstration clinics Professor Bull asked a student to give the history of the case, diagnosis, etc., which the young man did in most excellent English, evidently in honor of the presence of Americans in the clinic. I asked the student if he could do this in German, and he gave the history again in most beautiful German. He then repeated it in French, but less fluently. Professor Bull said that their students were required to speak at least three modern languages—Norwegian, English, and German; and that they were also expected to know French, and were excellent Latin scholars. The classes were limited in numbers, and the student body was exceptionally intelligent in appearance.

Professor Schilling is chief surgeon at the new City Hospital, which has about 1100 beds; and I saw with him many interesting cases. He speaks German and some English.

Professor Brandt has a new and very beautiful obstetric and gynecologic clinic, which is just completed. He teaches in the medical school, and has also a large school of midwifery for women who come there for a one- or two-year course. He speaks English.

From Christiania we went to Bergen, taking the day train through the mountains and getting off at Myrdal, just beyond Finse, where there is snow the year round, and where winter sports are carried on in summer. From Myrdal we went down through the Aurlands fjord, and back through the Maers fjord, and from here up the valley to Stalheim and on to Voss. These two fjords are part of the Sogne fjord, said to be the most picturesque in Norway. We also later had an excellent view of Hardanger fjord. The scenery in Norway is not surpassed by anything I have seen.

Bergen has a very fine hospital of 200 beds. The surgical department is under Professor Sandberg. This hospital has had given to it by Dr. Gads, a successful Christiania oculist, who was born at Bergen, a fine pathologic building. Dr. Haaland, the chief pathologist, was for several years with Bashford at the Cancer

Institute in London, and he is doing fine work in cancer research. Haaland finds that certain strains of mice are hereditarily susceptible to cancer, especially mice that are infected with nematodes, which have a great tendency to burrow into the soft tissues about the breast of the mice.

In Bergen is a leper colony containing about 250 lepers. Our knowledge of this disease was here greatly enriched by Hansen, who found the bacillus of leprosy. Bergen was the home of Grieg, the musician, and Ibsen, the author.

DENMARK

Denmark, with a population of about 2,000,000 people, has but one university, with about 4000 students, 500 to 600 of whom are in the medical department. This university is situated in Copenhagen, the one great city of Denmark, with somewhat more than 500,000 people. In the State Hospital, which has 1000 beds and is most modern and complete, Professor Th. Rovsing has charge of the surgical department. He is a man fifty-two years of age, who dominates Danish surgery by reason of his great originality and force of character. He is a kindly man, universally beloved, and yet he has fought for his opinions as only a strong man can fight who believes he is right. He has done most excellent original work, especially in connection with surgery of the kidney, and has one of the finest collections of urologic specimens I have ever seen. In speaking of the formation of the kidney stone, he said that these stones are probably congenital; that uric acid is often found collected in the tubules of the kidney of new-born babies is well known, as there is not always enough fluid to wash it away. If remnants remain, they may later act as nuclei for calculi.

Of recent years he is best known by his operation for prolapse of the stomach. I attended Sir Arbuthnot Lane's clinic with him in London last year, and after examining a number of cases of "stasis," Rovsing said: "These patients are exactly the same as I cured by operation for prolapse of the stomach, and this latter operation has the great advantage over colectomy, that it can be undone and is not dangerous to life." Professor Rovsing visited

America in 1912, and read a paper before the Surgical Section of the American Medical Association on "Gastrocoloptosis: Its Pathologic Significance and Its Surgical Treatment." I saw him do several of these operations, and I have no hesitation in saying that, if an operation is indicated for prolapse of the stomach, his method and technic are the best I have any knowledge of. Rovsing often combines this operation with a method of elevating prolapsus of the transverse colon. I saw him resect a stomach, uniting the end of the cut stomach directly to the side of the jejunum, after the method of Polya, of Budapest. He uses ether in a bag, putting in about one and one-half ounces, and it seemed to work well with this small quantity. I asked him what precautions they took in handling the ether in this way, and he replied with a smile, "When the patient gets blue, we take it away."

Rovsing uses aluminum-bronze wire as a continuous suture in closing the abdominal wall, and says that the copper in it renders it antiseptic, so that it is almost never necessary to remove it later and that it will heal into granulation wounds. This wire is as soft and pliable as silk, and is tied in quite the same way. Rovsing speaks English.

Professor Fenger Just is a nephew of the late Christian Fenger, of Chicago. He is chief surgeon to the Deaconess' Hospital, and has 100 beds. The hospital lies in a beautiful garden, and the clinic is interesting. Professor Just speaks English.

Professor Johnnes Kaarsberg is chief surgeon to St. Luke's Hospital. He is a fine operator, rapid and courageous. I saw him do a number of operations which elicited my admiration. He speaks English.

The finest hospital in the world is probably the new City Hospital, which has just been completed in Copenhagen. It is of the two-story pavilion type, and is laid out in a way to remind one of the World's Fair in Chicago, with its colonnades, flights of steps, etc. This hospital well repays a visit. Professor Wessell is the chief surgeon, and is an operator of skill and experience.

Dr. Graham was greatly interested here in the work of Professor Fibiger, who showed that cancer of the stomach is prevalent among

rats found in the sugar warehouses where American sugar is stored, and that the irritation which caused this cancer of the stomach was due to the nematodes harbored by the American cockroach. He was able to produce cancer of the stomach in rats by feeding to them cockroaches infected with nematodes, and in this way he added one more argument to the long chain of evidence as to the relation of chronic irritation to cancer.

Copenhagen is a most interesting city. It was here that Thorwaldsen, the great sculptor, lived and worked, and his models and many examples of his art are to be found in the Thorwaldsen museum. The Jacobson Museum has as fine a collection of statuary as I have ever seen. Here also Hans Christian Andersen wrote his beautiful stories, and his statue is to be seen in one of the parks.

I left the Scandinavian countries with regret that I could not remain longer. The high character of the people, their advanced civilization, and their splendid institutions fill one with admiration.

BELGIUM

Belgium has about 7,000,000 people, rather evenly divided between the Walloons of the south and east, who are essentially French and speak that language, and the Flemish, who speak modified Dutch. These two elements are in more or less constant strife. Just now the Flemish are in political control.

The city of Brussels contains 500,000 people, and is rather evenly divided between the Walloons and the Flemish. The court language is French, and French is much more extensively spoken in Brussels than Flemish. Brussels has three large hospitals, two of which are city hospitals containing 700 beds each, although the new one is not yet completed. There are four universities in Belgium with about 5000 students in all.

Professor Antoine Depage, who visited America in 1914 as President of the International Surgical Association, is Professor of Surgery in the Medical School. He is a very forceful man, who introduced asepsis into Belgium in contradistinction to antisepsis, and who also introduced trained nurses into his hospital, obtaining his nurses from the Denmark training-school. He speaks French.

Professor Depage uses spinal anesthesia to a considerable extent. I saw him do a number of operations. One was a colostomy after the method of Desquin, of Holland, with a single suture. The sigmoid was brought out through a lateral incision, and a very heavy silk thread introduced through the entire thickness of the abdominal wall on one side, through the mesentery of the exposed sigmoid, and from within out on the opposite side. The end of the thread was then passed back through the mesosigmoid, and the two ends tied tightly together. The incision was so nicely planned that this single thread brought the skin of each side, as well as the whole abdominal wound, into apposition at the center, except for the thickness of the mesentery, thus leaving just room enough for the bowel to enter and emerge on either side.

Depage has one of the most beautiful private hospitals I have ever been in. It has but 18 beds, and the personnel of its organization is at least 25 people. The installation is very complete, and could be carried out only in a land where labor is cheap. In America the cost would be prohibitive.

Professor Lorthioir is chief surgeon to the Children's Hospital. He is an excellent operator. I saw him do a number of herniotomies and appendectomies, taking but a few moments for each one. He has done some 1200 operations for the radical cure of hernia in young children. He never ties the sac. He draws it well out of the abdomen, cuts it off, and lets it slip back, and has never seen a relapse. He also has a very beautiful private hospital facing a little quiet square. I noticed a statue in this square, and, walking out to see it, found it to be of Vesalius, the anatomist, bringing to mind the fact that Vesalius had done his work in Brussels. Professor Lorthioir speaks French and a little English.

The country about Brussels is extremely beautiful, and only about 15 miles distant the battle of Waterloo was fought. It is one of the most interesting battle-grounds in the world, and the visit paid us well.

From Brussels we went to Antwerp, visiting on the way the old cities of Ghent and Bruges, of historic interest.

Antwerp is a Flemish city. Last year, in my random notes on

travel, I spoke of Lambotte, the surgeon of Antwerp, and his work on bones and on the stomach. I again had an opportunity to visit his clinic and witness him operate on several bone cases. His methods are exceedingly simple, working with few assistants, and his results are admirable.

One case in particular was especially interesting. A fleshy, alcoholic man, a poor risk, of about sixty years of age, had fallen from a height of 15 feet a week before, crushing the right elbow. The arm was much swollen and discolored. A long posterior incision was made, the olecranon sawed, and the joint, which was crushed into fragments, exposed. I thanked my stars that I did not have that joint to repair; and the patient might well have thanked his, for within twenty minutes, by introducing some screws of an original type, Lambotte had made a perfect restoration of the joint. No drainage was used.

Lambotte has resigned from the city hospital, where he had a large amount of this sort of work. He operates now only in private practice, and his material is therefore limited. I was very glad that I had notified him of my coming, thus giving me so excellent an opportunity to again see his work. He speaks French and a little English.

THE INFLUENCE OF EUROPEAN SURGERY ON AMERICAN PRACTICE*

WILLIAM J. MAYO

I am sure the members of the Southern Minnesota Medical Society feel it is a privilege to meet in Winona, the largest city in the district. As I drove my motor from Rochester this afternoon on the splendid concrete roadway, I could not but note how much Winona has done and how much she has stimulated the municipalities in her neighborhood to civic improvement and to better things generally. I remembered also with great pleasure two Trojans in the medical profession who belonged to Winona in the early days of Minnesota medicine. They were not only leaders in their profession, but ranked high in the community and in the love of their confrères. I refer to Dr. Franklin Staples and Dr. J. B. McGaughey. To these two, as much as to any men of the State, we owe our splendid medical profession. As I look back, I wonder if Minnesota did not have sturdier men in their day than at the present time.

Our Medical Practice Laws have made it possible to practise in this State with self-respect and an assurance of at least a moderate income. A condition quite contrary exists in some States, where the practice of medicine has been reduced until the members of the profession are too poor to provide the equipment necessary for giving satisfactory service to the people. What is worse, through lack of State control, some of these States have become a dumping-ground for the unfit—men of low ideals and poor education.

Because of these excellent laws, Minnesota has been able to bar

the half-educated men, and I am sure that much of the proud position that the State holds in the medical profession to-day, which I believe to be higher than that of the average State in this country, is due to the efforts of our pioneer physicians.

In considering the topic given me for this evening, I was reminded of an incident at a children's party in my house some years ago. The little ones were playing a game in which a child was blindfolded and two pieces of metal were struck together about his head. He was required to tell in what direction the pieces of metal were being struck. I was astonished to see that the sense of hearing was so defective that they were unable to locate the sound. I began to think about the question of the special senses and their relation to every-day life. We know, of course, that the first of the special senses developed is the sense of taste, so that improper food shall not be taken into the mouth. Then comes the sense of smell, to turn the mouth toward the food. Next the sense of hearing, which I have shown is so uncertain. None of these special senses is highly developed. Then comes the blessed sense of sight, which is the higher faculty of the mind.

What is it that has bestowed upon our people of to-day so varied an understanding—political, social, and scientific? It is the ten-cent magazines with their illustrations. An unintelligent person may gain comprehension of a situation by means of pictures and diagrams, which without them would not be understood. When all is said and done, we are superior to lower animals because the higher functions of the brain have direct paths to the sense of sight; in other words, the brain has been built about the sense of sight. Memory, with many of us at least, is largely photographic, and we reproduce things by psychic visualization.

John Hunter was the first man who systematically used the sense of sight in pathology. He was not only a great pathologist, but he had the modern spirit. When Jenner was trying to prove the value of vaccination by argument, Hunter wrote to him and said: "Why think? try it on a hedge-hog and know." Hunter had in his museum, which was 26 x 48 feet, a wonderful collection of postmortem and operative material which he showed his students.

To-day those who go to the Royal College of England will find all these specimens numbered in black and equal to anything we have produced in modern times.

I speak of this because in Hunter's day came respect for the medical profession, which, then, first began to deal with facts. As we deal with facts, we must stand or fall. As a result of the work of Hunter and his followers, England was the center of the medical sciences for half a century.

Scientific leadership passed from England to France. France was the first to study surgical anatomy consistently. Inspired with a desire to deal with the pathologic conditions which were shown to exist by John Hunter and his followers, the French developed surgical anatomy and a beautiful technic as compared with contemporaneous knowledge.

The coming of Pasteur was a great event. So far as the medical profession was concerned, it was the greatest event that has ever happened. The only man who can be compared with Pasteur is Charles Darwin, who revolutionized the natural sciences. Pasteur produced new facts, and produced them by the sense of sight, aided by the microscope.

The value of Pasteur's discoveries and their application to surgery was realized by Lister. Lister's work was first appreciated in Germany—not England. Lister had discovered that carbolic acid was useful in the treatment of wounds. He did not know why, until Pasteur's work showed him, and his own acute intellect at once built upon the germ theory the modern surgical structure.

The center of medical science has been successively England and France, and now it is Germany, because Germany first appreciated the great facts connected with Pasteur's and Lister's discoveries. Germany has done more and better work in the medical and surgical sciences not because the German mind is superior to the English, French, Scandinavian, or Latin mind, but because Germany has better organization.

Modern surgery was brought from Germany to America by many men, foremost among them Nicholas Senn, Christian Fenger, and Arpad Gerster. Senn was a natural leader because he taught

scientific truth in a popular way.   Fenger was also a leader, in a different way.   It was difficult to hear Fenger lecture until one became accustomed to his manner.   His written lectures were classics of English.

Fenger left a school of surgery, and from him Murphy, Ochsner, Harris, Billings, and many others in the West received their inspiration.   He may be said to be the father of modern surgery in the West.

Gerster taught by word and deed, and his book on "The Technic of Aseptic and Antiseptic Surgery" did more to modernize American surgery than any publication with which I am acquainted.

The cavities of the body were a sealed book until the father of modern abdominal surgery, Lawson Tait, and our own Joseph Price, carried the sense of sight into the abdominal cavity, as did Sir Victor Horsley and Harvey Cushing into the cranial cavity, and Willy Meyer, Meltzer in America, Sauerbruch, Friedrich, Tuffier, and many others showed the actual conditions existing in the thoracic cavity of the living.

With this inspection of the great cavities of the body much superstition of the old times disappeared.   The old practitioner settled down in his easy chair and thought he would not be disturbed, and younger men came along and cried "Fire!" and he had to get up to see if anything was burning.   The new knowledge burned up pelvic cellulitis, innocent gall-stones, and 35 supposititious diseases disappeared when the appendix and its infections were correctly interpreted.

Then Roentgen brought forth the x-ray, and the sense of sight enabled us to look into other hidden places of the living body, and what a wonderful effect upon our knowledge of human ills was brought about by the discoveries of this quiet German professor!

Germany is the only country which can be said to have a national school of surgery, and from it we have profited greatly. Germany has given us more than all the other countries together, but the German school is German made; they have learned little from the world at large.

I have often been asked if there is an American school of sur-

gery. It does not exist in the way we could say it exists in Germany. We have in America a great number of scientific travelers who have brought home the good from every land. Our surgery is cosmopolitan, based on the best in all countries, improved upon and made a part of our practice. American practice is too broad to be national. It had the scientific spirit, and science knows no country.

Within one hundred years we have seen the leadership of medical science pass from England to France, from France to Germany. Modesty prevents me from naming the country to which it will go next.

THE HOSPITAL AS AN EDUCATIONAL IN-STITUTION*

CHARLES H. MAYO

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The development of the modern hospital has been an achievement of the present generation. To be sure, hospitals of some sort had been in existence probably as long as higher intelligence had existed in the human race. They had been developed to care for the poor and the friendless of large communities, and were patronized only by those of the better classes who lived at considerable distance and came to secure the services of a physician or surgeon of great reputation, or because there was none available at their homes. Consequently the greater capacity of the hospital was in wards, and the few private rooms were for isolation and moribund patients. Hospitals were then the social meeting-place of all varieties of germ life, of which danger the profession was ignorant, and hospital gangrene was very common among the injured and those operated on.

Asylums for the insane were more in the nature of prisons than hospitals—their caretakers were jailers. Although long ago the chains were struck off from the unfortunate inmates, there was but little about such institutions to give confidence that those confined therein would ever sufficiently recover to be released.

For a hundred years there had been but little progress in medical treatment. What made the great stimulus to hospital development? It was Lister's appreciation of the work of Pasteur concerning germs, their growth, the results of their activity, and the methods of destroying them. This knowledge, applied to medi-

cine and especially to surgery, revolutionized the practice of medi-
cine.   As the science of surgery developed, a new zest was given to
the study of the body and its diseases.   By the application of these
principles the dangers from surgery were minimized, and it became
possible to study disease, infections, and growths in their varying
stages in the living; their life-history became known, and methods
of cure were developed.   While the study of the dead had taken the .
science of medicine far, it now advanced by leaps and bounds.   It
was shown that the diseases which terminated long illnesses were
often to be avoided, since they were due to secondary and compli-
cating conditions.   As science and art developed in the old hos-
pitals, new institutions sprang up like mushrooms the world over,
since the applied idea was essentially institutional.   The public
began to appreciate the fact that better care and closer supervision
could be obtained in a hospital than in a private home, and indeed
that *only* in such institutions could the best care be given them.

Second only in importance to the medical staff of a hospital is
its nursing corps, and much of its reputation depends on the effi-
ciency of the nurses.   In the old days, outside of denominational
hospitals, especially in Europe, nurses were constantly changing,
and were often recruited from among the unfortunate girls and
homeless women too active to warrant being supported either in a
poor-farm or workhouse.   This made it more difficult to secure
girls of the better families and higher intelligence abroad to take up
the profession of nursing.   The condition is now changing in Eu-
rope, and within the past few years a great improvement has been
made in this regard.   In our newer country, not bound down by
traditions, nursing has always been looked on as a noble profession,
and, when hospital activity developed some thirty years ago, mak-
ing such tremendous strides, the training schools were filled with
the best young women of our nation.   The training these women
receive, coming as it does after a high school or college degree, is a
liberal education in itself.   The instruction in domestic science
and the care of the sick, the general knowledge of disease, especially
the care of contagious and infectious diseases, will add much to the
development of our country in the influence exerted on it in later

life by nurses and ex-nurses as members of civic bodies that demand protection for children, school inspection, and an efficient public health service which insures pure food and drinking-water and perfected sanitation.

Europe is far ahead of us in the establishment of large hospitals supported by the city, the provinces, or the Government. The hospital there is considered an economic institution of great value, that the sick, injured, deformed, and crippled be as completely and quickly restored to health as possible. In all the countries of Europe the care and protection of the individual stand far in advance of the attention devoted to agriculture. In our country we have a secretary of agriculture as a member of the cabinet, but there is no cabinet officer who has the conservation of human life in his charge. This subject rests with the public, and the influence that can be exerted on public opinion by the few who have special knowledge.

While there is no national control of public health, there are hospitals in a few States which are a part of the university system, and which are for the better training of students on whose knowledge of medicine will depend the future conservation of the health of its people and also for the training of nurses. Those who live in Minnesota are to be congratulated, first, on the inherent wealth of the State and the fact that its public lands, held for educational purposes, were held as State property through the honesty of our State officials of an early day. The school iron lands of Minnesota are returning an increasingly great amount of money to be used for educational purposes. We have had for many years one of the finest universities, and have recently established the nucleus of a university hospital, with an efficient training-school for nurses. The State superintendent of public instruction of New York has said that our university hospital training-school system for nurses is the best planned in America.

Our State hospitals for the insane are of the highest order. The mentally deranged are admitted as sick patients and treated as such until they can be without question placed in the class of curables or incurables. Considering what has been done for the mentally deranged, it is but a step to see in the future the establishment

of hospitals for the cure of drug habits,—morphin, cocain, and the like,—and of asylums for the treatment of the inebriate: inasmuch as the State licenses, as a business, institutions for his destruction, it is thereby in a sense responsible to him.   Drug-stores should be licensed, as they frequently supply both drugs and liquor to the mentally deficient, and only in this manner can they be effectually controlled by the possible loss of their license.   In this class I would include the self-dispensing physician.

The control of contagious and infectious diseases is much easier, since special hospitals have been established for their care.   Those who have been patients in these institutions have gained and dis- seminated knowledge of such diseases, and laws are thus more easily enforced with regard to their control, being supported by public opinion.   It is fairly well understood now that such dis- eases should be under control and that the so-called diseases of childhood are not necessary.   Many States, Minnesota among them, have established sanatoria for the care of the tuberculous. Those who live in sanatoria even for a time are less a menace to others because of the knowledge they acquire of disease and its causes.   The public will shortly insist that bovine tuberculosis can and must be prevented.

HOSPITAL EFFICIENCY

Hospitals are State, city, denominational, charity, and private. Their responsibility to the State seems to terminate with the yearly report, which is usually of a semi-advertising character.   Truth- ful as hospital reports may be in a general way, they are only fairly valuable as statistics.   While indicating to a certain extent the character and amount of work performed, they are of far more value to those directly concerned in the work of the institution than of any special value as education to the profession.   There should be a uniform system of keeping records, to be examined periodically by a hospital inspector as to their efficiency, and such inspector should be paid by the State.   In the first development of an institution a low mortality is quite a necessity.   Later in its life a higher mortality—far from indicating, for example, poor sur-

gery—often indicates a greater effort by a more radical operation to secure permanency of cure; also indicates an acceptance for treatment of those in whom disease is far advanced, rather than condemning them to suffering and death without effort at relief.

Codman, in an endeavor to make hospital reports of more value, propounds a series of questions to be asked in the individual case as follows:

"What was the matter? Did they find it out beforehand? Did the patient get entirely well? If not, why not? Was it the fault of the surgeon, the disease, or the patient? What can we do to prevent similar failures in the future?"

He divides all results of surgical treatment which lack perfection to be explained by one or more of the following causes:

"Errors due to lack of technical knowledge or skill; errors due to lack of surgical judgment; errors due to lack of care or equipment; errors due to lack of diagnostic skill."

He says these are partly controllable by organization. Failures or partial failures come from patient's enfeebled condition, unconquerable disease, and refusal of treatment, conditions which are partly controllable by public education. There are certain calamities of surgery considered as accidents and complications over which we have no control.

Given an efficient hospital, when should a patient be placed in it? First, for medical treatment, those with acute diseases should receive hospital care at once, that they may derive all the benefits of the combined experience and knowledge of the staff of the institution. Those with chronic incurable diseases should be in the institution only long enough positively to determine the character and extent of the disease and its prognosis, and to give instruction for the care of the individual by himself at his home or by his home physician, that he may maintain his ambulatory condition and thus his independence as long as possible. It is as unfortunate to lean on an institution for the relief of chronic disease as to be condemned to a crutch.

SURGICAL CASES

After the diagnosis is made, a surgical patient should enter the hospital but one or two days preceding his operation, preferably the day before, unless it is necessary that he be for a time under medical observation or preparation.

To answer the question, "What was the matter and was it found out beforehand?" in the present day means efficient team work. It is practically impossible for a single individual to have the personal ability to carry out all the technical detail of both the general and the special examination; in fact, the possible complications may readily prevent a correct diagnosis, except for the efficient team work of specially trained observers. Surgical judgment and ability come of experience. Surgical technic requires constant observation and travel if one is to keep abreast of progressive thought.

MORBIDITY

The morbidity of patients has received marked attention in the study of hospital output and efficiency.

PERIOD IN HOSPITAL

In the work at St. Mary's Hospital, of the approximately 1000 operations on the appendix and allied organs in the past year, the period in the hospital was barely one week. It is not many years ago that patients were confined to bed three weeks after removal of the appendix. The shorter confinement shows a saving, not to the hospital, but to the patients, of two thousand weeks during the year, or the full capacity of a 40-bed hospital for a year. Again, operations on the bile-ducts and the gall-bladder formerly necessitated a stay in the hospital of three to four weeks, yet over 800 such cases in 1913 averaged less than two weeks in the hospital, a saving of one bed for approximately thirty-five years; and thus efficiency of output in hospitals, as in any other industry, marks progress. It is claimed by some, more especially those who conduct private hospitals, that those patients do better who are kept a long time in bed and are built up slowly. This is not, however,

in accord with the facts, which are that more than a week in bed cannot be spent without a great lowering of the blood-pressure, that the early ambulation of patients prevents this lowering of blood-pressure and minimizes the heretofore unpreventable complication of pulmonary embolism classed as accidents of surgery. It can be shown that the convalescence is immeasurably reduced by limiting the bedridden period to the shortest possible number of hours, and protecting wounds by deep sutures, to be left for a week after the patient is up. As soon as possible, surgical patients should leave the hospital and go to some private home or sanatorium, where they will be surrounded only by patients similarly affected on the road to recovery, and the psychologic benefit of this is of enormous advantage. While the large hospitals of Europe, with their spacious grounds, lend themselves to the outdoor life and movement of the individual, the hospitals of our country do not have such advantages as the closed grounds of these magnificent parks. Here they are commonly situated on expensive ground, in densely populated and noisy locations, where only emergency hospitals should be placed. To overcome this handicap, many of the hospitals could build convalescent homes outside of the city, and others should sell the valuable business property and rebuild or convert it to business purposes as an income to support a modern hospital properly located.

To keep a patient in the hospital longer than is necessary is an unwarranted expense to him or an unjustified tax on those who contribute to hospital expenses, besides keeping some other needy patient from being cared for.

Hospitals are seldom conducted on good business principles. Some members of the board are placed there because they will contribute or are good money-getters, and others because of influence. Too often these members are like the business directors who don't direct. When hospitals can be standardized and a Taylor system of efficiency of management be secured, a wonderful improvement will ensue.

Surgical judgment is born of experience in most instances, but could be more quickly and safely acquired if some large hospitals

would but give the after-results of certain operations, as, for instance, fixation of the uterus in young married women.   This would probably indicate, not the discarding of the procedure as a method, but of its non-use in certain years of life.   Why should not the sex organs of the female receive the same consideration for preservation as the male in neurasthenia?   Has the average physician ever considered how few questionable procedures are made upon the external body?   They are mostly hidden conditions, and often buried.   A hospital should be responsible for correct records of all operations and treatments of patients who enter the institution. This should be made by the superintendent, registrar, or intern, and kept, not for public inspection, but as a record for increasing hospital efficiency.   This does not prevent the surgeon from also keeping private records.   Such a record, with the percentage of success and failure, and the answers to the questions propounded by Dr. Codman, would give valuable information to be placed before a board of directors, and might lead to the question of why certain surgeons make so high a proportion of curetments and what necessitates such treatment.   The report showing the mistakes in diagnosis and the number of patients who came back for a second operation because the first did not benefit would be instructive.   The number who have evidently more than one trouble, the presence of which could so easily have been found by observation at the time of the first operation, becomes a serious matter when we think of the lost time, double risk, and burden of expense thrust unnecessarily on such patients or on the community.

The character of many operations would lead the board to suspect certain members of the staff of securing much of their business by a secret division of fees.   With directors, great improvement could be made by dropping members from the staff or advising others to take special courses in medicine or surgery.   It is to be hoped that within the next five years the College of Surgeons of America will do much to raise the standard of American surgery, and make a high standard of efficiency and honesty the ideal of the student of medicine.

SUGGESTIONS FOR WRITERS OF MEDICAL PAPERS

MAUD H. MELLISH

I. NOTES ON THE CONSTRUCTION OF MEDICAL PAPERS*

Notwithstanding the many excellent suggestions to writers already published,† it seems worth while, even at the risk of repetition, to place on record a few of the methods which, in our experience, have been found most useful.

TOPIC

In selecting a topic for his paper, the young author is subjected to varying influences, the most unfortunate of which is his conviction that he "must write something." This usually leads to his accepting, without realizing the amount of work involved, an invitation to read a paper before a society. In such case the paper should be written from the most available material at hand, and that which is most suitable for the audience and the occasion. Not only should the author choose his topic from the most available material of which he has made some original study, but, what is of greater importance, he should choose it from material of which he may have an opportunity to make further studies and investigations. Too often the young physician overlooks this point or considers it impractical, and in his haste to appear in

* Submitted for publication September 22, 1914. Reprinted from Journal-Lancet, 1915, xxxv, 33–34.

† For example, Allbutt, T. Clifford: Notes on the Composition of Scientific Papers, Macmillan & Co., London, 1904. Manly, J. M., and Powell, J. A.: A Manual for Writers, Chicago, 1913. American Medical Association: Suggestions to Medical Authors, Chicago, 1914.

print prepares his first of a series of widely disconnected papers, which are the result of a wasteful misdirection of his energy and but assist in further burdening with unrelated data an already overburdened medical literature. The author should early appreciate the fact that not only his surest means of recognition by his professional associates, but also his surest means of ultimately adding somewhat to the sum-total of scientific knowledge, lies in the thorough and persistent study of a single subject, rather than in a desultory study of many subjects. In a series of articles giving the results of continued observations on the same topic material already published should not be repeated. The author must particularly guard against this practice. A brief summary or a reference to previous articles is quite sufficient for the intelligent reader.

TITLE

The title of a paper should set forth the character and extent of the ground covered in the article, not only to enlist the attention of the interested reader, but also for the convenience of future reviewers and bibliographers. Valuable material is often hidden under a casual or irrelevant title. If only a limited phase of the subject is to be discussed, *e. g.*, the surgery, the limitation should be stated. *The title should be a concise and brief index of the material under discussion.*

MEDIUM OF PUBLICATION

While the chosen audience determines not only the subject, but the phase, method, and scope of its development, it is conversely true that the chosen subject determines the audience and the journal in which the paper should be published. This is especially true when it is desirable to announce without delay a new method or a new discovery. The deplorable custom of publishing miscellaneous articles in journals purporting to cover only special subjects and of publishing special articles in journals covering a miscellaneous field is not only wasteful of the reader's time, but also is a persistent annoyance to the reviewer compiling data on a particular topic.

It is not within the scope of this paper to make a plea for the reduction of the number of journals, for the more sharp limitation of their fields, or for the appointment of editors with full authority to accept or reject material according to their best judgment. The time is coming, however, when a general movement toward these ends must be made by the entire medical profession.

Length of Papers

A paper should be brief and clear, demanding only enough of the time and patience of the audience to permit the presentation of the essential points. The practice in some of our medical societies of reading only abstracts of articles, thus giving more time for the discussion of a subject, might well be adopted more generally. It is worthy of note that an abstract will usually be found to contain all that is essential of the original article. Orations for special occasions may occupy more time, but, even under such circumstances, it is better to err on the side of brevity. Special papers not intended to be placed before an audience may contain observations, results of investigations, and descriptions of interesting cases more in detail. However, should an article necessarily extend beyond 5000 words, it may be wise to publish serially or in a monograph. If published serially, an opportunity is also afforded for more complete investigation of the subject.

Arrangement of Notes

Assuming that the author has completed his studies on his own material, that he has familiarized himself with the literature on the subject, and that he has made careful notes on cards or sheets, the next step is the arrangement of such notes in logical working order. They must be classified according to the plan best adapted to the presentation of the author's own work, and this may necessitate a further subdivision of his notes on the literature. *Definiteness, accuracy, and uniformity in reference scannot be too strongly urged.* Time is saved in recording data and making abstracts at the time literature is read.

OUTLINE

Following such an arrangement, the next step is the construction of a definite framework on which to build the body of the paper. The importance of making a complete outline will always be appreciated after it has once been done. While outlines must be varied according to the subject under discussion, in general the following may be adapted to almost any scientific subject: ·

A. *Introduction.*—This should give the object of the paper, the character and extent of the original data to be discussed, and the sequence of the article, if it be one of a series.

B. *Historic.*—This should give a review of the literature of the subject, restate briefly the author's own previous studies, if any, and, when possible, summarize the views of contemporary workers in the same field.

C. *Material and Methods.*—This should include an exact statement of the character and amount of material investigated, of the old and new methods of solving the problems, and of the operations, devices, etc.

D. *Results.*—Here should be given a detailed discussion of the results of the investigation, operative procedure, or experimentation. While findings which prove the author's working hypothesis may properly be given first place in the argument, other findings of a negative character and those of no apparent significance should also be stated.

E. *Summary and Conclusions.*—A brief restatement should be made of the work done and of the conclusions which may properly be drawn therefrom. The author should have in mind that this portion of the paper is usually not only the first portion read, but that it may be the only portion read. Further, if properly made, the summary and conclusions may serve as a most desirable form of abstract to be published by other journals.

FIRST DRAFT

Having completed the outline, the first draft of the paper should be made. If possible, it should be dictated to a stenographer who is familiar with medical terms. Should it be necessary to make

it in handwriting, care should be taken to write legibly, leaving wide margins and wide spacing to permit changes and notes of instruction. The use of the dictaphone is obviously more rapid than writing by hand, and perhaps no more difficult when once learned than dictating to a stenographer, since both methods require practice. A quiet place with sufficient space to spread out notes and papers should be selected for dictating or writing. All available precautions should be taken against interruption, which is clearly detrimental to inspiring or consecutive thought. In writing or dictating from the classified notes and references the outline of the paper should be closely followed. Dictating from memory leads to inaccuracies in statements and to faulty construction.

REVISION

On a clean typewritten copy of the first draft of the paper, with wide margins and spacing, one should be able to do all necessary revising, patching, and polishing. The paper should have several careful readings, for the following purposes:

1. Changes in the arrangement of the material. If the outline has been properly made and faithfully followed, few changes may be necessary.

2. Additional data, ideas, missing links in the argument, etc.

The author cannot be too careful in this portion of the work to eliminate inaccuracies and incomplete statements, unverified data and statistics, incorrect proper names, dates, numbers, and bibliographic references.

3. Proper placing of illustrations and subheadings, and the order of arrangement of bibliographic references. While the headings may be determined by the outline, they may frequently be best inserted after the first draft of the paper has been made.

4. A final review of the diction. In this review a fine discrimination must be exercised in the choice of words, in the arrangement of phrases, and in general in the consideration of the impression which will be conveyed to the hearer or reader. For example, if the writer will imagine himself in the place of the reader or the audience, he will be quick to note how frequently a

strong point is weakened by repetition. A speaker may safely drive his point home by repeating once, while a second repetition is always fatal. A writer may not effectively repeat save in other words.

Criticism.—After the paper has been revamped, pruned,. and elaborated, it should be rewritten, and then, if possible, laid aside for several days, when it should again be reviewed by the writer. Following this, it should be submitted to the criticism of others, who should revise it from the standpoint of subject matter and also of equal importance from the standpoint of diction. If only minor changes are made, they may be inserted in typewriting. If, however, extensive changes are made, it will be best to make a clean copy of the paper before submitting it for publication. In any event the final copy of the paper should be at least in duplicate, the original being sent to the publisher and the second copy held for proof.

II. ON THE USE OF THE REFERENCE LIBRARY IN THE PREPARATION OF MEDICAL PAPERS*

Introduction.—The accumulation and review of medical literature as a preliminary step in the preparation of medical papers is often a perplexing experience, particularly to the younger men of the profession, who may, as yet, have had little practice in such work. With the enormous volume of medical literature now being published, it is a heavy task for the skilled librarian, even with her familiarity with the many excellent indices and catalogues, to collect the titles alone of significant literature concerning any particular phase of a topic. What, then, must it be for the young physician who is unskilled in the use of catalogues, who does not readily recognize such articles as may possibly contain valuable material bearing on his subject, and who also may not know the scientific standing of the various journals?

The librarian is conversant with the books and periodicals of

the highest standing. She may even be conversant with the subject-matter of the articles contained therein, and she is often asked for detailed information, regardless of the fact that supplying such details may be quite outside of her legitimate duties. The demand for skilled assistants in the collection and review of papers has resulted in the development of professional reviewers, bibliographers, abstracting bureaus, etc., furnishing data to physicians who lack the training, the time, or the material necessary to collect and make such reviews for themselves. There is need also for the skilled employee of the library, who is familiar with medical literature, and who works in immediate association with the physician, aiding him in the collection, selection, and translation of articles, and in making stenographic notes of his abstracts.

Without entering into a discussion of the question as to whether to the librarian, to the professional bibliographer, to the skilled special assistant, or to the physician himself shall be left the task of accumulating and selecting medical literature preliminary to its final critical analysis by the author,—a question which must be determined in each instance by the local conditions,—I venture to make a few suggestions from the editorial standpoint which may aid in systematizing the details incident to the composition of medical papers.

Reference Lists.—Whatever their motives, most physicians find it necessary, as a part of any investigation, to acquaint themselves with the methods of previous workers, their facts and their conclusions, and, finally, to select from these such as may bear on the solution of their own problems. The first logical step, therefore, is a compilation of a list of titles of papers which may yield the desired information. Perhaps it is not sufficiently well known among physicians that, of the numerous indices, catalogues, reviews of current literature, year-books, etc., the most useful are the *Index Medicus*, the *Index-Catalogue of the Surgeon General's Library*, the *Guide to Current Literature* of the Journal of the American Medical Association, and the *Supplement* to *Surgery, Gynecology and Obstetrics*. For periods not covered by these, and

for articles from related sciences, *e. g.*, physics and chemistry, of course, other sources of information must be consulted.

When reference lists are prepared by employees of the library, they should be as complete as possible and be made on standard index-cards. Those references selected by the physician should be copied on standard-size thin cards or on sheets large enough for his notes. Only the original cards should be filed in the library.

Selection of Significant Articles.—When the list of titles has been thus compiled, it will be found to contain references to the work of a few known men and to that of many unknown men whose articles have been published in a few journals of unquestionable standing and in many of very questionable standing. Thus, oftentimes, a large number of the references may be wholly ignored; and, in any event, the articles in standard periodicals by recognized authorities should be consulted first.

Of the approximately 1600 medical journals now published, a very small number contain the original reports of the bulk of the really important work done by the medical profession. The occasional worthy article found in the remaining journals is usually a simultaneous publication, a series of abstracts, or the report of an isolated case. While it may sometimes be of interest to the physician to read articles composed principally of uncritical reviews, he should accept their conclusions with discretion, since careful scrutiny very often reveals in them inaccuracies in data and reasoning. The harmful custom of quoting such articles and passing them on, frequently diverging further and further from the truth, as well as assisting in the perpetuation of their original errors, cannot be too strongly condemned. As a rule, the study of a few original articles containing in minute detail the results of painstaking investigation, and accompanied by good illustrations, is worth more than the hasty review of innumerable inaccurate compilations.

Thus at the outset the attention of the physician may be readily concentrated upon a relatively limited number of articles, many of which should be found even in the small medical library. Frequently, however, some of the articles included in the list which

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seem to be significant will need to be obtained from other libraries, from the authors, or from publishers direct. Further, when these articles are finally obtained, many of them must be translated into English. The physician who has not actually experienced the difficulties of accumulating his own reference literature will find it hard to be patient, with the attendant delays. Fortunately, the courtesies so generously extended by the greater medical libraries to those of us in charge of smaller libraries do much to reduce these delays.

Abstracts and Translations.—What shall be said concerning the use of abstracts made by bureaus for a specific topic? While there are fewer objections to their use than to the use of abstracts prepared for general information only, and while they may be sufficiently accurate for the collection of statistical data, the fact must be borne in mind that, aside from a personal interview with the author, nothing can give so true a conception of his interpretation as a careful study of the original report. Needless to say, if material is obtained through the medium of abstracts only, it should not be incorporated into papers without stating its immediate source.

The use of translated abstracts is, of course, even more to be deplored than the use of abstracts of English articles. Literal translations of entire articles, however, are trustworthy, and quite necessary when the physician is unable to read the language in which the original report was published.

Order of Study.—Physicians sometimes do not take into consideration the fact that the order of development of a subject is rarely the order in which it should be studied. In general, the physician whose experience has not already taught him another routine should review the more recent articles first. In this way he not only quickly acquaints himself with the contemporary point of view concerning the subject in hand, but, also, he may find references to other valuable data bearing on the topic, but reported under titles giving no clue to their relationship, and therefore not previously included in his reference list.

Notes and Bibliographies.—The physician should make his

notes and reviews on standard cards or sheets provided for that purpose; and they should be preserved at least until his article is completed and the bibliography verified. Completeness and accuracy in notes and bibliographic reference will save a great deal of time and trouble for the author, as well as for the editor.

In the final list of references for publication, the quotation of authorities not personally reviewed, and the inclusion of direct references to them, are to be avoided. This unfortunate practice, which has grown up from thoughtlessness on the part of writers, is not only time-wasting, but also misleading, since it conveys the impression that the author has based his conclusions upon the study of the original articles. An author who feels it necessary to refer to work of which he has seen only a review, should always make this clear in the body of his paper.

Study-tables.—Whenever literature is reviewed in a reference library, study-tables should be provided in the stack-room, permitting ready access to the shelves for immediate consultation of articles other than those already selected, but which may have some bearing upon the subject. Where space permits, it is best to assign a table to each worker, of which he may have exclusive use for an extended period. In addition, when possible, it is desirable to place tables in separate rooms or alcoves, giving privacy for the dictation of papers, abstracts, etc.

The preceding suggestions are based upon several years' experience in a small library used freely by a limited number of physicians in the preparation of medical papers. While they may not be of interest to the trained investigator who has already developed a system of work, they may prove of some value in assisting the young author who also recognizes the importance of a definite system in his preliminary literary investigations. They may be summarized as follows:

SUMMARY

1. There is a demand for skilled assistants to collect and review medical papers. Some of these should be employees of the library who are familiar with medical literature, who are skilled

stenographers, and who work in immediate association with the physician.

2. The first step in the review of medical literature is the compilation of as complete a bibliography as possible from the current indices, catalogues, etc., these to be on standard cards, which should be preserved for use in subsequent investigations of the same topic.

3. Original articles in standard journals by well-known authorities should be read before reviews and abstracts.

4. New or final conclusions should not be drawn from abstracts and reviews alone.

5. So far as scientific medicine is concerned, the thorough study of recent literature is of more importance than the random review of early literature.

6. Notes and references should be systematically and accurately made on standard-size cards or sheets, which should be preserved by the physician at least until his paper is published.

AN APPARATUS TO ASSIST IN THE APPLICATION OF DRESSINGS ABOUT THE HIP*

H. W. MEYERDING

In applying dressings, especially of plaster-of-Paris, in the region of the hip-joint a rest is needed which will add to the patient's comfort, allow sufficient working space, give a feeling of security during traction, permit easy removal, and leave a well-fitting cast.

Patients not infrequently complain more of pain during and following the application of a cast than of the disease which required its application. Orthopedic surgeons find plaster a more serviceable dressing because they have learned, through experience, to guard against the pitfalls attending its use. Sores due to pressure may be avoided by padding and smoothness of the areas of contact. The sacrum is one of the most common sites of such sores, mainly the result of flat, ill-fitting appliances which leave irregular irritating areas supporting the weight of the body.

In order to insure perfect contact and avoid pressure-pain, the support should conform to the lumbosacral curve, and allow as large a weight-bearing area as possible. Since a bone plate or graft may be loosened during the application of a cast, ease of application and removal are also important. An apparatus that will allow a certain amount of traction without slipping is also essential.

To meet these various requirements, casts of the lumbosacral region were taken of patients of varying ages in the prone position, and a support of average size designed by the writer, which has
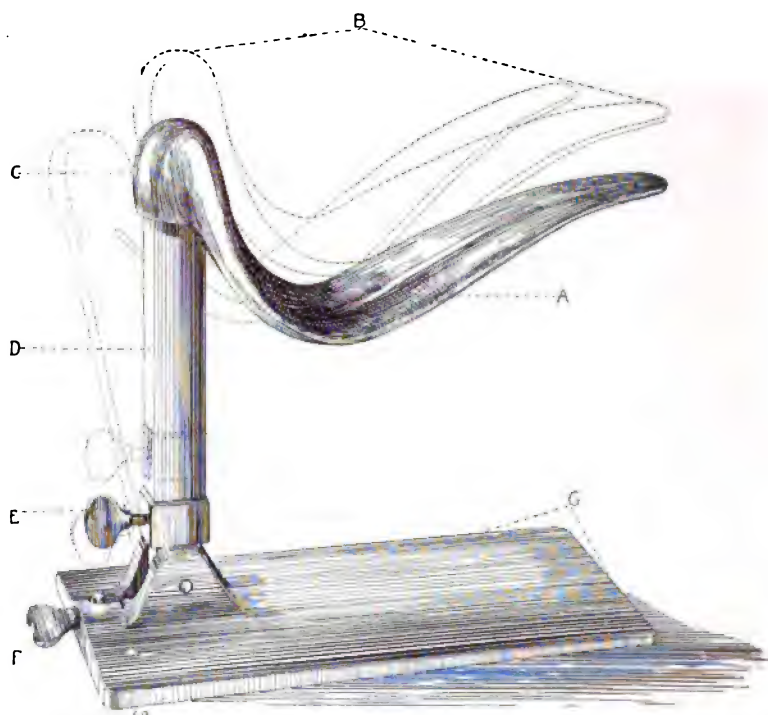
Fig. 344.—Removable rest (A) used to support cast while hardening. The various degrees of elevation of the tongue are shown; B, elevated position; C, a square joint which prevents rotation and allows traction against the perineum; D, a hollow rectangular bar to obtain elevation, fixed by a screw (E); F, screw fitted in heavy base (G) by means of which the bar (D) is tilted and the tongue lowered or elevated.
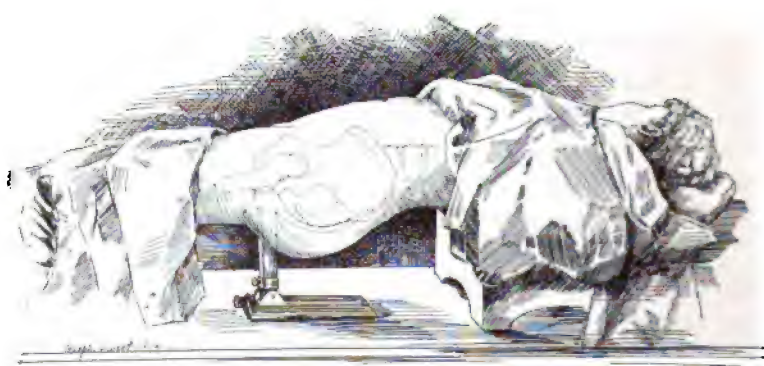
Fig. 345.—Sacral rest in position.

been used with satisfaction in the Mayo Clinic for the past three years.   The apparatus is removable and can be left under the cast while hardening takes place.   It may be lowered or elevated so as to meet varying degrees of tilting, *e. g.*, as are found in ankylosis of the hip, and allows traction against the perineum (Fig. 344).

The patient is placed in position as shown in Fig. 345. The parts to be covered are encased in stockinet, the bony prominences are well padded with felt, then a single layer of flannel in the form of a bandage, after which the plaster bandages are applied.   Trimming is done with the patient resting on the support; the flannel is allowed to protrude one-half inch beyond the plaster, the stockinet is drawn up over this and the rounded edges of the cast, and held in place by a gluten bandage.

SOME NEW CAMERAS FOR LABORATORY USE*

LOUIS B. WILSON

I have recently completed two cameras for laboratory use, and in describing them also include two others which have been in use for some time.

I. Camera for Use with Proctoscope

This camera (Fig. 346) consists of a cylindric barrel (*A*) to the front end of which is attached a rapid, short-focus, photographic
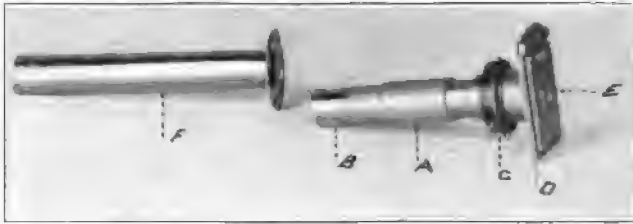
Fig. 346.—Camera for use with proctoscope: *A*, Tube; *B*, lens; *C*, shutter; *D*, receiver; *E*, plate-holder; *F*, proctoscope.

lens (*B*), and to the other end of which are attached a simple photographic shutter (*C*) and small metal receiver (*D*) for taking a plate-holder (*E*) which carries an ordinary photographic plate 4.5 by 6 cm. in diameter.

In use, when a desirable field is found through the direct-vision proctoscope (*F*), the camera is inserted with the shutter closed and set for time exposure, and the dark slide of the plate-holder drawn. The patient's buttocks are steadied, the shutter

snapped, and an exposure of from two to five seconds given.   The shutter is then closed and the camera withdrawn from the proctoscope.   The operation should require not more than twenty seconds, and interferes but slightly with the ordinary course of a proctoscopic examination.   The resulting pictures are circular and $1\frac{1}{8}$ inches in diameter.   The chief difficulty encountered is in

Fig. 347.—Miniature camera for photomicrography: *A*, Box; *B*, shutter; *C*, light-tight sleeve; *D*, receiver;   *E*, plate-holder.

maintaining the patient in a fixed position for the few seconds necessary to make an exposure.

II. Miniature Camera for Photomicrography

Laboratory workers have for a long time experienced great inconvenience in having to carry a microscopic slide from the

microscope which they ordinarily use to one set up and adjusted for photography. A number of cameras have been devised to obviate this difficulty. With but two exceptions, these have all required the use of a large heavy plate on which the microscope rests at all times, or to which it must be transferred after the desired field is found. Of the two exceptions, one is a camera which fits directly on the draw-tube of the microscope, weighs 685 gm. (23 ounces), and uses a plate of a size difficult to obtain in America. The other is a camera which has a very heavy base, and while the whole apparatus may be moved up to the microscope, yet has no means of rapidly centering the two. The miniature camera here described and the larger portable camera to be described next both get rid of the inconvenience of the heavy soleplate, and yet work with simplicity, speed, and accuracy.

The miniature camera (Fig. 347) consists of a pyramidal aluminum box (A), bearing at one end a shutter (B) with a light-tight connecting sleeve (C), and at the other end a receiver (D) which takes a plate-holder (E) carrying a plate of the ordinary blocknote size, 4.5 by 6 cm. The whole apparatus is 9 inches long and weighs, complete, as it goes on the microscope, only a trifle over 7 ounces. In use, when a desirable field has been found in the microscope, the camera is slipped on the microscope, to which it fits securely by means of a sleeve that remains permanently on the draw-tube. The camera is placed in position with the dark slide drawn and the shutter set for a time exposure and closed. The focus is then adjusted an amount previously determined by the fine adjustment screw, the shutter opened and the exposure made. The shutter is then closed and the camera removed from the microscope. The whole operation may be done without in the least jarring the microscope. Aside from the time of the exposure, which, of course, varies with the kind of light used and the magnification, the entire process requires less than a minute. This little camera gives excellent results, though its field of usefulness is, of course, limited by the small size of the plate and by the short range of magnification resulting from its short, fixed extension.

III. Medium-sized Portable Stand and Camera for Photomicrography

This stand and camera (Fig. 348) have been devised to get rid of the inconvenience of the sole-plate or other special stand to which the microscope has hitherto been attached when used for photomicrography. The new features in it are: (1) a tripod base (A)
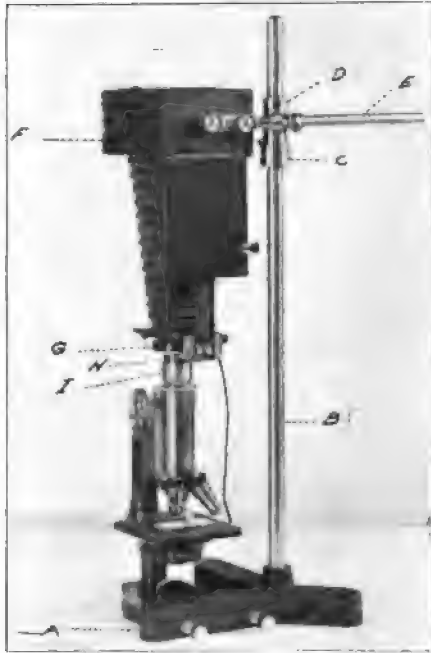
Fig. 348.—Portable stand and camera for photomicrography; A, Base; B, support; C, collar; D, reducing clamp; E, arm; F, camera; G, shutter; H and I, sleeve.

which can be adjusted accurately by set-screws to any microscope with the ordinary horseshoe base, so that the instrument, while not attached in any manner to the microscope, can be brought instantly into accurate alinement with it; (2) a supporting rod (B) carrying a collar (C) and clamp (D), the latter of which is specially constructed for holding a round horizontal arm (E) in a manner that will permit its being turned at any angle and yet held

with great firmness without turning; and (3) the camera (*F*) carried by the horizontal arm, by means of which it may be adjusted to any position from vertical to horizontal or tipped at any desired angle.

The camera itself takes the ordinary plate-holder for $3\frac{1}{4}$ by $4\frac{1}{4}$ plates, but is heavily reinforced in its working parts and has an unusually long bellows. A shutter (*G*) and light-tight sleeve (*H*) are attached to the front board. In use, the microscope to which the camera has been previously adjusted and to which is permanently affixed only a small inconspicuous part (*I*) of the light-tight sleeve may be used anywhere on a fairly level table. When a desirable field is found, the entire stand and camera are moved into position so that the studs and set-screws are in contact with the base of the microscope, when it will be found that the two instruments are in exact alinement. The readjustment of the focus may be made ordinarily with low powers by the fine adjustment screw, or, if necessary, with high powers, by refocusing on the ground glass. The subsequent steps of taking the photograph are those ordinarily employed.

The camera may be rotated on the support-rod at will, and brought again into exact alinement by means of two stop-studs—one on the collar and one on the clamp—which engage with each other. It may be used with the microscope in the horizontal position or inclined at any angle, though the instantaneous alinement is obtained only when the instrument is in the vertical position.

Photographic lenses may be added to the shutter, and the camera very conveniently used for photography of specimens and apparatus, or for making portraits, etc., while it is still attached to the stand. Or the camera may be detached entirely from the stand and then forms a high-class folding pocket camera suitable for plates or film-pack. For use with extra-long-focus lenses, I have had this camera built with a 16-inch extension which is obtained by means of a supplementary bed.

IV. LARGE STAND AND CAMERA FOR PORTRAITS, GROSS SPECIMENS, AND GENERAL LABORATORY WORK

Six years ago Andrews and I built and described * a large stand and camera for photographing pathologic specimens submerged. This apparatus has proved to be thoroughly satisfactory in our hands, but there is a demand for a more portable and withal a less
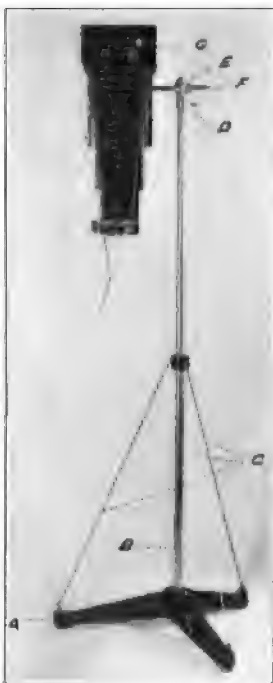
Fig. 349.—Large stand and camera for specimen and general laboratory photography: *A*, Base; *B*, support-rod; *C*, guy-rods; *D*, collar; *E*, right-angle clamp; *F*, arm; *G*, camera.

expensive machine to serve the same purpose. I have therefore devised the stand and camera shown in Fig. 349. This apparatus, which is well adapted for taking portraits of patients, photographs of gross specimens or operations, and for general photographic laboratory work, consists of a heavy tripod base (*A*) into which is screwed a heavy support-rod (*B*) 5 feet high, which is reinforced and

* Jour. Med. Research, 1908, xvii, 437.

made more rigid by three small guy-rods (C) running from a collar near its middle point to the ends of the feet of the tripod. On the support-rod are carried a collar (D) and right-angle clamp (E) which is specially bored to hold securely at any angle a round arm (F) with a forked end to which is attached an ordinary long-extension 5 by 7 folding box camera (G). The camera may be used in the vertical position, as when photographing specimens under water, horizontally, as for portrait work, or inclined at any angle, as in taking photographs of operations, apparatus, etc. Hardened steel domes are inserted at the bearing points of the tripod in lieu of the usually unsteady casters. The whole apparatus is portable, light, simple in construction, and extremely rigid, while its cost is very low.

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